KATHOLIEKE UNIVERSITEIT
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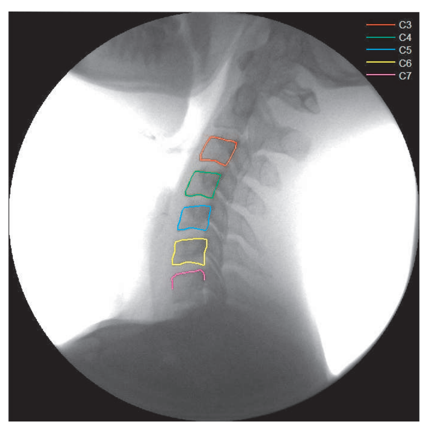
Arenberg Doctoral School of Science, Engineering & Technology
Faculty of Engineering
Department of Mechanical Engineering

Biomechanical analysis of total cervical disc prostheses

Joris WALRAEVENS



Dissertation presented in partial fulfillment of the requirements for the degree of Doctor in Engineering

December 2010

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Joris WALRAEVENS

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UDC 61

December 2010

D/2010/7515/129
ISBN 978-94-6018-290-7

Dankwoord

> We can't solve problems by using the same kind of thinking we used when we created them. Albert Einstein

Als ik een thesis voor het eerst in mijn handen neem, is het dankwoord een van de stukken die ik het eerst en misschien zelfs het liefst lees. Een niet te onderschatten stukje tekst dus want het is de ideale gelegenheid om iedereen te bedanken die er voor gezorgd heeft dat ik dit werk met vrucht kon afwerken tot de finish heb volgehouden. Bij sommige kon ik rekenen op de fysieke bijdrage van hun nek; anderen hadden eerder een technische of emotioneel ondersteunende rol.

Op de eerste plaats wil ik mijn promotoren prof. Jos Vander Sloten en prof. Jan Goffin bedanken. Zij hebben me geïntroduceerd in de fascinerende wereld van de biomechanica. Zij zijn een mooi voorbeeld van hoe ingenieurs en artsen op een vruchtbare en amicale manier kunnen samenwerken.
Beste prof. Vander Sloten, dank u wel voor uw pragmatische aanpak en voor de verantwoordelijkheid en het vertrouwen dat u me gunde. Als ik door de bomen het bos niet meer zag, was u er om me de goede richting uit te sturen.
Beste prof. Goffin, dank u wel voor al de tijd die u voor me vrijmaakte om me in te wijden in de intrigerende wereld van de neurochirurgie. Uw gedrevenheid, kritische kijk en expertise hebben me naar een hoger niveau getild zowel op intellectueel als op persoonlijk vlak.

Hartelijk dank aan prof. Hugo Hens, prof. Harry van Lenthe, prof. Herman Bruyninckx, prof. Paul Suetens, en prof. Paul Anderson om deel uit te maken van mijn jury. Jullie kritische maar constructieve opmerkingen waren onontbeerlijk voor dit werk. Prof. Anderson, both surgeon and engineer, you are the real embodiment of multidisciplinarity. Thank you for being part of my jury.

Furthermore, I would like to thank Medtronic (Memphis, USA) for the institutional research and education grant that provided me the possibility to do this research. Special thanks to Megan Harper, Frank Chan, Mark Dace, Daniel Baker, Jeff Rouleau, Newt Metcalf and Alison McConnell. Your scientific expertise and feedback were very valuable for me. I could not have done this without you.

Zoals in elk multidisciplinair onderzoek is dit werk het resultaat van een nauwe samenwerking van heel veel mensen. Ik wil al de mensen van het Universitair ziekenhuis Gasthuisberg bedanken die een bijdrage aan mijn onderzoek hebben geleverd: allereerst Dieter Seghers en prof. Paul Suetens van het Centrum voor Spraak en Beeldverwerking, voor hun belangrijke bijdrage bij het ontwikkelen van het bewegingsanalyse algoritme; Jan Leemans, Guido Pauwels en Walter Coudijzer, van de afdeling Radiologie, voor hun paraatheid, hulp en enthousiasme bij de radiografie- en CT-studies; en Jo Verbinnen en prof. Paul Herijgers, van de afdeling Anatomie, voor hun hulp bij de kadaverexperimenten. Vervolgens wil ik ook prof. Bart Depreitere, dr. Hans Delye, prof. Philippe Demaerel en dr. Joke Meersschaert bedanken voor hun medewerking bij het valideren van de scoresystemen. Tenslotte wil ik ook Isabelle van Hoof, dr. Jeroen Ceuppens, prof. Bart Depreitere, prof. Johan van Loon, en dr. Frank Van Calenbergh, van de afdeling Neurochirurgie. vermelden voor hun enthousiasme, hulp tijdens de experimenten of voor hun suggesties over de klinische aspecten van deze thesis en de voorgaande presentaties.

Uiteraard wil ik ook mijn collega's van BMGO bedanken voor hun belangrijke bijdrage. Rita, dank je wel voor de niet aflatende steun en hulp. Jij bent de rots in de branding bij BMGO. Daarnaast wil ik Pieter, Ivo, en Stefan bedanken voor hun technische ervaring en inputs. Zonder jullie had ik de ontwerphindernissen nooit zo vlot kunnen nemen. Tenslotte wil ik iedereen op BMGO bedanken die het leven en werken er zo aangenaam maakt, in het bijzonder, Bert, Nele en Vincent. Jullie waren er bij vanaf het begin en ik ga onze -soms hilarische- momenten missen.

Ik wil graag alle mensen bedanken die vrijwillig hun nek hebben uitgestoken voor mij en die mee actief op zoek zijn gegaan om anderen daartoe te overtuigen. Jullie onbaatzuchtige hulp is heel belangrijk geweest voor dit onderzoek.

Naast al deze wetenschappelijke bijdragen zijn er ook een hele boel mensen die op andere vlakken hebben bijgedragen tot dit doctoraat. Zij zorgden ervoor dat het leven naast het onderzoek altijd sportief, gezellig, en uitdagend was. Een dikke merci aan de vele vrienden en aan mijn broers, Jasper en Stijn.

Ik wil ook enkele heel speciale mensen bedanken. Moeke en papa, zonder jullie motivatie, steun en warme thuis was ik er nooit in geslaagd om te geraken waar ik nu ben. Al 27 jaar hebben jullie mij op weg geholpen en geïnspireerd. Met enige trots kan ik jullie hiervan vandaag een resultaat tonen. Anke, lieve schat, wat zou ik zonder jou moeten beginnen? Als het eens minder vlot vooruit ging, stond je altijd klaar om me te motiveren en weer in de goede richting te wijzen. Jij vult me perfect aan en prikkelt me om boven mezelf uit te stijgen. Samen kunnen wij alles aan.

Joris
Leuven, 16 December 2010

Abstract

Biomechanics of cervical disc prostheses are a young and multidisciplinary research discipline. Due to the constant quest for innovation, cervical arthroplasty is on route to revolutionize the treatment of cervical degenerative disease. But distinct guidelines for favorable patient inclusion criteria are needed. Moreover, surgical techniques should be optimized to achieve high prosthesis placement accuracy. Through a close collaboration between engineering, medicine and industry, this PhD tried to answer some of the questions regarding cervical disc replacements that were raised in literature.

First, the necessary measurement tools and techniques were developed and validated. A motion analysis algorithm for calculating lateral intervertebral continuous motion patterns in the cervical spine was established. An existing tool, which has proven its value in numerous studies, served as a benchmark in the validation process. Next, two separate objective scoring systems to qualitatively and quantitatively assess the degree of cervical intervertebral disc degeneration on lateral radiographs and facet joint degeneration on CT scans were developed and validated.

Using these tools, five studies were conducted to answer some of the raised questions regarding favorable patient inclusion criteria and accurate surgical techniques. Firstly, quantitative and qualitative motion patterns of the cervical spine during flexion/extension, lateral bending and axial rotation were measured and calculated. This was done for asymptomatic volunteers of different ages to investigate a possible correlation between disc degeneration and intervertebral motion.

Secondly, a prospective assessment of the intermediate and long-term radiographic characteristics of disc replacement surgery with the Bryan Cervical Disc was completed. In this study radiographic features such as postoperative mobility, discus degeneration and heterotopic ossification were longitudinally analyzed and their effect on clinical outcome evaluated.

Thirdly, quantitative and qualitative motion patterns of patients operated with

a Bryan Cervical Disc Prosthesis were compared with those of the control group of healthy volunteers, to investigate whether an intervertebral disc prosthesis can mimic normal and physiological motion patterns.
Fourthly, postoperative segmental alignment was studied between two cohorts of 20 consecutive patients operated with a Bryan Cervical Disc Prosthesis in a retrospective radiographic study. In one of the groups, patients with severe preoperative kyphosis were excluded and the surgical technique was slightly altered in order to avoid asymmetric overdrilling of the posterior part of the cranial endplate of the vertebral body.
Fifthly, the postoperative in vivo position of cervical disc prostheses of a consecutive series of patients was quantified in a retrospective radiographic analysis. The influence of a malplaced prosthesis on the biomechanics of the cervical spine was investigated using a three-dimensional, non linear finite element model.

The results presented in this work indicated that patient selection is indeed critical. Foremost, preoperative mobility is influenced by pre-existing intervertebral disc degeneration. Moreover, preoperative mobility of the index level increases the chances for the prosthesis to remain mobile after surgery. Furthermore, patients with a mobile prosthesis tended to do better clinically.
Additionally, preoperative segmental kyphosis proofed to be baleful for proper postoperative alignment. For a successful cervical disc replacement surgery, the following inclusion criteria should be followed: (1) the patient should have a preoperative mobile index level; (2) the patient should have minimal pre-existing degeneration at the index level; (3) the patient should have a lordotic alignment prior to the surgery.
The results also showed that accurate implant positioning is essential to guarantee long term functioning of the prosthesis and good clinical outcome. A correct surgical technique is crucial to obtain good postoperative segmental alignment. Although, malplacement showed to have little effect on the mobility at the index and adjacent levels as well as on the stresses at the intervertebral discs, at least in the circumstance predicted by the finite element model, prosthesis malplacement predisposes to accelerated facet joint degeneration at the operated level, and eventually neck pain in the future.
The surgical accuracy which is needed to obtain good clinical results was however not addressed in this thesis. This multidisciplinary research collaboration was merely a first, but indispensable, step towards the confirmation of current research questions of patients, surgeons and industry. In this PhD, several tools were developed and results discussed which serve as a solid base for future research.

Korte Inhoud

Het onderzoek naar de biomechanica van de cervikale discus prothese is een jong en multidisciplinair vaarwater. Dankzij de voortdurende queeste naar innovatie, is cervikale arthroplastie (i.e. ingreep waarbij de discus vervangen wordt door een prothese) goed op weg om de behandeling van degeneratieve ziekten van de nek te revolutioneren. Om dit te realiseren moeten strikte richtlijnen opgesteld worden over inclusiecriteria voor patiënten. Bovendien moeten chirurgische technieken geoptimaliseerd worden om een hoge nauwkeurigheid te garanderen tijdens het plaatsen van de prothese. Vanuit een samenwerking tussen ingenieurs, artsen en industrie, probeert deze thesis een antwoord te geven op sommige van deze vragen die in de literatuur gesteld zijn.

In eerste instantie werden meetinstrumenten en -technieken ontwikkeld en gevalideerd die nodig waren voor dit onderzoek. Zo werd een algoritme uitgedacht om laterale intervertebrale bewegingspatronen op te meten op basis van radiografieën. Een bestaand algoritme, dat gebruikt werd in meerdere klinische studies, diende hiervoor als vergelijkingspunt. Daarnaast werden twee objectieve scoresystemen ontwikkeld en gevalideerd om discusdegeneratie en facetdegeneratie kwantitatief en kwalitatief in kaart te brengen aan de hand van radiografieën en CT-beelden.
Deze meetinstrumenten werden vervolgens in vijf verschillende studies gebruikt om een aantal vragen naar gunstige inclusiecriteria en chirurgische technieken te beantwoorden. Eerst werden kwantitatieve en kwalitatieve bewegingspatronen van de nek bestudeerd bij flexie/extensie, laterale buiging en axiale rotatie. Dit gebeurde voor asymptomatische vrijwilligers met een brede waaier van leeftijden om een mogelijke correlatie tussen discusdegeneratie en intervertebrale beweeglijkheid te onderzoeken.
Vervolgens werden de radiografieën van patiënten, bij wie een discusprothese werd geïmplanteerd, prospectief onderzocht, zowel intermediair als op lange termijn. Dit onderzoek spitste zich voornamelijk toe op een bestaande prothese, namelijk de Bryan Cervikale Discus prothese (Medtronic). De beweeglijkheid

van de prothese, discus degeneratie en heterotropische ossificatie werden gecorreleerd aan klinische resultaten.
In een volgende fase van het onderzoek, werden de kwantitatieve en kwalitatieve bewegingspatronen van de patiënten vergeleken met die van de controlegroep van gezonde, asymptomatische vrijwilligers, om te beoordelen of de intervertebrale beweging van een prothese het normale en fysiologische bewegingspatroon kan nabootsen.
Vervolgens werd in een retrospectief, radiografisch onderzoek, de intervertebrale houding van de nek bestudeerd bij twee cohorten van 20 patiënten, allen geopereerd met een Bryan Cervikale Discus prothese. In de eerste groep werden de oorspronkelijke inclusiecriteria en chirurgische techniek gehanteerd. In de tweede groep werden de inclusiecriteria strikter gemaakt: patiënten met een uitgesproken preoperatieve kyfose kwamen in niet aanmerking voor de operatie. Bij deze groep werd ook de chirurgische techniek gewijzigd om het asymmetrisch overmatig wegfrezen van het posterieure deel van de craniale eindplaat te vermijden.
Ten slotte werd de in vivo positie van cervikale discus protheses in kaart gebracht aan de hand van een retrospectieve radiografische analyse. De invloed van een misgeplaatste prothese op de biomechanica van de nek werd onderzocht aan de hand van een driedimensionaal, niet-lineair, eindig-elementen model.

De resultaten in deze thesis tonen aan dat inclusiecriteria voor patiënten inderdaad belangrijk zijn. Ten eerste, preoperatieve beweeglijkheid wordt negatief beïnvloed door discusdegeneratie. Daarenboven verhoogt de beweeglijkheid van een discus voor de operatie de kans dat een prothese ook na de operatie gedurende lange tijd mobiel blijft. Patiënten met een beweeglijke prothese doen het over het algemeen klinisch beter. Ten tweede, een slechte uitlijning van het geopereerde niveau kan vermeden worden als kyfose voor de operatie gezien wordt als een contra-indicatie voor cervikale arthroplastie. Voor een geslaagde discus vervangende operatie kunnen dus de volgende selectie criteria in acht genomen worden: (1) de patiënt moet een beweeglijk index niveau hebben voor de operatie; (2) de patiënt mag slechts beperkte discus degeneratie op het index niveau hebben; (3) de patiënt moet lordose van de nek hebben.
De resultaten in deze thesis tonen ook aan dat een nauwkeurige plaatsing van de prothese cruciaal is om het functioneren van de prothese en de klinische resultaten ook op lange termijn te garanderen. De juiste chirurgische techniek is essentieel om een goede lordose van de nek te blijven garanderen na de operatie. Een misgeplaatste prothese heeft weinig effect op de beweeglijkheid van de prothese of op de spanningen en rekken in de intervertebrale disci. Een misgeplaatste prothese vergroot daarentegen wel de kans op versnelde degeneratie van de facetgewrichten en dus op nekpijn in de toekomst.
De chirurgische nauwkeurigheid die nodig is om goede klinische resultaten te

behalen kwam in deze thesis niet aan bod. Dit multidisciplinair onderzoek was slechts een eerste, maar noodzakelijk stap naar het beantwoorden van de huidige vragen van patiënten, artsen en industrie. Bijkomend onderzoek is nodig. In deze thesis werden de nodige meetinstrumenten ontwikkeld en resultaten geboekt die als basis kunnen dienen voor verder onderzoek.

List of Symbols and Abbreviations

$\alpha"(v,v+1,i)$	rotation of vertebra v with respect to vertebra $v+1$ in frame i
$\theta_{v,i}$	orientation of the region of interest round vertebra v in frame i
$\mathbf{C}_{v,i}$	contour of vertebra v in frame i in the ROI reference frame
$\mathbf{C}'_{v,i}$	contour of vertebra v in frame i in the original image reference frame
$\mathbf{R}(\theta_{v,i},\mathbf{t}_{v,i})$	planar transformation matrix of vertebra v in frame i
$t_x"(v,v+1,i)$	anteroposterior translation of vertebra v with respect to vertebra $v+1$ in frame i
$t_y"(v,v+1,i)$	craniocaudal translation of vertebra v with respect to vertebra $v+1$ in frame i
$\mathbf{t}_{v,i}$	location of the center of the region of interest round vertebra v in frame i
$\mathbf{W}$	diagonal weighting matrix
X,Y	pixel coordinates

aDI	disc insertion angle
aFSU	angle of the functional spinal unit
ALL	anterior longitudinal ligament
AP	anteroposterior
AR	axial rotation
CAM	continous angular motion
CL	capsular ligament
COR	center of rotation
CT	coronal tilt

CTM	continous translation motion
EZ	elastic zone
F	female
FE	flexion/extension
FEM	finite element model
FL	flaval ligament
FSU	functional spinal unit
GAP	gap between the anterior rim of the prosthesis shell and the vertebral body
HO	heterotopic ossification
ICC	intraclass correlation coefficient
ICP	iterative closest point
IDP	intradiscal pressure
ISP	intraspinous ligament
IVM	intervertebral motion
LB	lateral bending
M	male
ME	measurement error
NR	not reported
NZ	neutral zone
OM	out-of-midline
PLL	posterior longitudinal ligament
QMA	quantitative motion analysis
ROI	region of interest
ROM	range of motion
RSA	roentgen stereophotogrammetry
SD	standard deviation
Ti	titanium
TR_x, TR_y	anteroposterior and craniocaudal translation

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Chapter 1

General introduction

The research field of the biomechanics of cervical disc prostheses is relatively young and brings together neurosurgeons, orthopaedic surgeons, and engineers in search of mobile implants which might serve as an alternative for interbody fusion after anterior decompression, for patients who are diagnosed with intervertebral cervical disc disease.
This chapter lists the convention that are used throughout this thesis. Moreover the kinematics and biomechanics of the cervical spine of healthy individuals and of patients with an intervertebral disc prosthesis are discussed. In addition, the need for grading systems for the degeneration of cervical intervertebral discs and facet joints is explained. Finally, the voids in the relevant literature are pointed out.

1.1 Introduction to cervical spine arthroplasty

The human cervical spine supports, orients the head and protects the spinal cord. The cervical spine consists of seven vertebrae connected with soft tissues, such as ligaments, intervertebral discs and muscles. The ligaments and the articular facets joints restrict excessive movement of the cervical spine. The intervertebral disc acts as a shock absorber and together with the synovial joints ensures articulation of two vertebrae with each other. For a more elaborate description of the functional anatomy of the cervical spine, this chapter references to White and Panjabi [154].

Degeneration of the intervertebral disc is one of the most frequently encountered spinal disorders [145]. Degenerative disc disease of cervical spine can cause combined symptoms of neck pain, radiculopathy, i.e. nerve root compression which may result in pain, weakness and numbness of the upper extremities, or difficulty controlling specific muscles, and/or myelopathy, i.e. spinal cord compression causing pain and may lead to paralysis [3, 117]. During the last 50 years anterior cervical decompression and fusion (ACDF) has become the gold standard in the treatment of patients with cervical disc disease. In the United States approximately 125.000 ACDFs are performed each year. The use of ACDF however, still has several disadvantages [27, 31, 35]. Long term data (up to 10 years) suggest that there are significant radiographic and clinical consequences associated with fusion. Firstly, it converts a functionally mobile spinal unit into a fixed, non-functional one. Secondly, it has been hypothesized that increased biomechanical stress and intradiscal pressure at these adjacent segments, together with the loss of shock attenuation at the treated level, may lead to an accelerated degeneration of the adjacent segments. This hypothesis is supported by clinical follow-up data, radiological studies, and biomechanical and mathematical models [48, 49, 58, 96, 121, 155]. Thirdly, pseudarthrosis is reported to occur as the result of failure of fusion [162]. Finally, pain and discomfort can be associated with spinal fusion, particularly with the harvesting of an iliac graft [86].

It has been suggested that cervical disc replacement surgery, after anterior decompression, eliminates the problems associated with fusion [3, 7, 134]. Recently, cervical biomechanical and clinical studies have shown that a cervical intervertebral disc prosthesis might preserve, or even restore, functional motion at the operated level, thereby maintaining adjacent level kinematics and reducing the rate of adjacent level degeneration when compared with intervertebral body fusion [23, 27, 31, 45, 122, 149, 155]. Longer term follow-up studies will have to prove that cervical disc prostheses are able to take over the role spinal fusion has played.

1.2 Definitions and general conventions

This section lists the definitions and conventions that are used to characterize the biomechanical behavior of the human cervical spine and its anatomical components. These conventions will be used throughout this thesis.
The orthogonal right-handed coordinate system (figure 1.1) that is used throughout this thesis was originally presented by White and Panjabi [154]. The origin of this coordinate system is placed at the geometric center of the vertebral body, which is assumed to lie in the midsagittal plane at the intersection of the diagonals connecting the superior anterior corner with the inferior posterior corner and the superior posterior corner with the inferior anterior corner of the vertebral body.
A functional spinal unit (FSU) is the smallest fundamental part used to characterize the biomechanics of the cervical spine. A FSU comprises of two adjacent vertebrae with the surrounding soft tissue: intervertebral disc, uncovertebral joints, facet joints and ligaments, but devoid of musculature [26]. The influence of the absence of musculature is discussed in section 1.3.2. The biomechanical behavior of a FSU is similar to that of the entire spinal column, which may be considered as a series of stacked FSUs. Within a FSU, the upper vertebra moves relative to the lower vertebra, which is fixed.
To describe the biomechanics of a FSU using external loads and displacements, two opposite forces or translations along each axis or two opposite moments or rotations about each axis are necessary. In total six forces and moments and six translations and rotations document the mechanical behavior of a spinal unit (figure 1.1).

1.3 Kinematics of the middle and lower cervical spine

1.3.1 Introduction

The kinematics of the cervical spine can be studied by investigating the intervertebral motion (IVM) within each functional spinal unit (FSU). This thesis mainly focuses on IVM; global motion of the cervical spine, defined as the motion of the head with respect to the thorax, is discussed minimally.

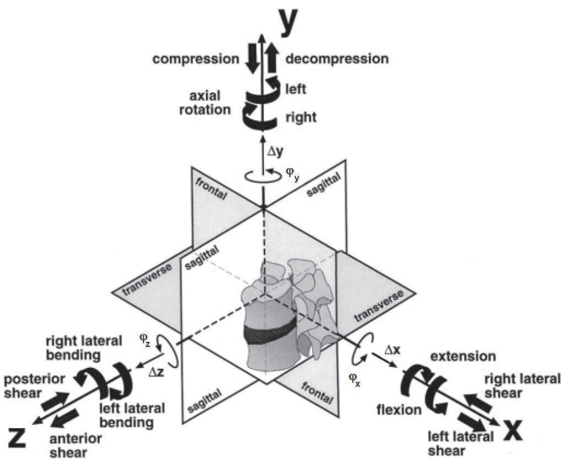

Figure 1.1: Definition of the three-dimensional coordinate system with 6 possible loads (3 forces and 3 moments) and displacements (3 translations and 3 rotations). Adapted from Wilke et al. [160].

1.3.2 Measuring in vivo kinematics

Numerous studies measured global ROM of the cervical spine using potentiometers [33, 37, 95], inclinometers [92, 144], optoelectronics [38, 136] or more recently ultrasound [16, 32, 91, 92, 95, 143]. The main benefits of these measurement techniques are that they are noninvasive; they can be used in clinical practice; and they can provide three-dimensional motion. However, these studies measure the ROM of the head with respect to the thorax and not intervertebral motion. Chen et al. provided an overview of three-dimensional global ROMs measured using the aforementioned different measurement techniques [18]. Based on this review the cervical spine's global range of motion is approximately 35° to 76° of flexion, 33° to 93° of extension, 39° to 61° of lateral flexion, and 49° to 97° of axial rotation to both sides. These results show a large variability between different studies. This variability might be due to differences in measurement protocol, e.g. active versus passive motion, or due to a discrepancies in age of the test population: the mean age of the test groups differs from 25 to 65 years [18]. Moreover, global motion of the neck does not necessarily reflect the movement among vertebrae in the cervical spine. In fact, a vertebra may experience its greatest ROM in flexion or extension before the cervical column itself has fully flexed or extended, e.g. a vertebra may experience a large range of movement in one direction while the cervical column on the whole exhibits movement in the opposite direction [94].

Previously, cadaver studies were the only alternative to quantitatively obtain three-dimensional IVM data. However, the lack of physiological tonus of musculature makes the results of in vitro studies incomparable to intervertebral motion measured in vivo [13, 66].
MRI, radiostereography and (bi-planar) radiography are alternative methods to measure intervertebral motion in vivo:

- Duerinckx et al., and more recently Ishii et al. provided in vivo three-dimensional intervertebral range of motion data using MRI [30, 64, 65, 66]. High accuracy was obtained, up to 0.24°. A major drawback of measuring motion patterns of the cervical spine using MRI is that no realtime kinematics can be recorded; acquisition times ranged from about two seconds to five minutes for every position. Moreover, in the aforementioned studies the patient/volunteer was in a supine position during measurement. Kuwazawa et al. found posture dependent differences in the cross-section of the cervical cord between patients measured in supine and erect position [81]. Therefore it might be hypothesized that the position of the patient influences the motion patterns of the cervical spine. To establish a normal database using MRI, the motion patterns of the volunteers should be measured in an erect position as the weight of the head and the surrounding stabilizing musculature might influence the motion patterns.

- Roentgen stereophotogrammetry (RSA) can provide precise in vivo three-dimensional intervertebral measurements, but requires invasive implantation of markers to accurately track movement of the vertebrae [83, 87]. Measurement accuracies in the lateral plane up to 0.7° and 0.2 mm can be obtained. Due to the invasive nature of this measurement technique only patients in the postsurgical situation can be assessed.

- Miura et al. [100] and Iai et al. [63] reported three-dimensional motion of the cervical spine using biplanar radiography. The accuracy of this method depends on the accuracy of identifying identical landmarks on separate frames of the same vertebra, which is not easy to achieve [13]. Iai et al. achieved accuracies up to 1.0 mm for translations and up to 1.5° for axial rotation.

- The most frequently used method to assess the IVM is based on lateral radiographs or lateral fluoroscopy. Most of the studies reported results based on data retrieved from two frames, representing maximum flexion and maximum extension [39, 40, 108, 125, 126]. Data on the intermediate positions to measure e.g. continuous angular motion (CAM) and continuous translational motion (CTM) is limited. Van Mameren et al., Hino et al. and Goffin et al. studied continuous cervical motion using fluoroscopy or cineradiographs [51, 59, 93, 94, 150], thereby using data from the intermediary frames.

The reliability of a measurement technique can be reported using the inter- and intraobserver errors, expressed using e.g. measurement errors [12] or intraclass correlation coefficients [139], next to the technical accuracies that can be obtained [13]. Table 1.1 summarizes the accuracies, intra- and interobserver errors during in vivo intervertebral motion analyzes of different measurement techniques.
The overall error of radioscopic as well as of radiostereographic measurements depends on the accuracy to track identical landmarks for each vertebra in the different frames. This is a very labor-intensive, time consuming and error prone work when done manually. Some authors use semi-automatic, computer assisted tracking software such as KIMAX QMA (Medical Metrics Inc., Houston, TX) [51, 125, 126] or developed their own computerized semi-automatic motion analysis software [39, 118] to track the vertebrae of interest. However, a motion tool that is on-the-spot useable in daily clinical practise and that is user-undemanding is not available up to date.

1.3.3 Intervertebral motion data

Many authors have presented data in support of the hypothesis that abnormalities in IVM provide important diagnostic information in the evaluation of patients reporting neck or related complaints [4, 39, 62, 126, 150]. Motion patterns can also be used as an outcome measure for spinal manipulations, adjustments and other treatments [17]. Furthermore, IVM can be useful as a benchmark to compare postoperative IVM after cervical arthroplasty and might serve as input for the development of finite element models.

Intervertebral motion of healthy individuals

Bogduk and Mercer provided an excellent overview of qualitative and quantitative motion patterns of the human cervical spine [13]. Ordway et al. [108] and more recently Reitman et al. [126] and Frobin et al. [39] used lateral radiographs or fluoroscopy to assess normal full flexion and extension IVM data of healthy individuals.
Table 1.2 provides an overview of lateral intervertebral ROM. This table shows a large variability within each study and between the studies separately. This variability might be due to differences in measurement protocol, e.g. active

Table 1.1: Accuracies and intra- and interobserver errors during in vivo intervertebral motion analyzes using different measurement techniques.
RSA: Roentgen stereophotogrammetry, rot: rotation, TR: translation. †normalized to mean vertebral depth. FL/EX: flexion/extension, LB: lateral bending, AR: axial rotation, NR: not reported. * Based on a study of the motion patterns of the lumbar spine.

author	Method	FL/EX	LB	AR	TR	intraobs		interobs		Ref
							Rot	TR	rot	TR
Reitman et al.	radioscopy	0.5°-1.4°	/	/	0.3 (max 1.4) mm	NR		0.85°	0.53 mm	[125, 126]
Frobin et al.	radioscopy	1.1°-1.9°	/	/	0.02 (max 0.03)†	1.91°	0.03†	1.98°	0.05†	[40]
Dvorak et al.	radioscopy	0.76°	/	/	0.3 mm	NR		NR		[34]
Iai et al.	biplanar radiography	3.0°	4.5°	1.5°	1 mm	NR		NR		[63]
Mimura et al.	biplanar radiography	1.5°	1.5°	1.5°	1.0 mm	NR		NR		[100]
Ishii et al.	3D MRI	0.24°	0.31°	0.43°	0.52 mm	NR		NR		[64, 66]
Leivseth et al.*	3D RSA	0.7°	0.2°	0.3°	0.2 mm	NR		NR		[83]

Table 1.2: Summary of in vivo intervertebral ROM using lateral radiographs or fluoroscopy.
Ante: anteflexion motion from full extension to full flexion; retro: retroflexion motion from full flexion to full extension; †no direction was specified. M: male, F: female. Results are presented in degrees (SD or min-max).

		C2-C3		C3-C4		C4-C5	
author	**number**	**ante**	**retro**	**ante**	**retro**	**ante**	**retro**
Van Mam. et al.	M+F: 10	**13.6** (10.5-15.0)	**13.1** (10.3-15.4)	**17.6** (12.9-21.6)	**17.6** (12.7-21.6)	**20.1** (14.9-23.9)	**20.7** (15.1-24.7)
Ordway et al.	M+F:20	**13.0** (4.8)	**6.5** (5.2)	**16.6** (3)	**8.3** (5.1)	**19.0** (3.1)	**9.5** (3.9)
Reitman et al.	M+F: 140	/	**9.9** (3.7)	/	**15.17** (3.2)	/	**16.9** (3.8)
Penning et al.	M+F: 20	**12** (5-16)†		**18** (13-26)†		**20** (15-29)†	
White et al.		**10** (5-16)†		**15** (7-26)†		**20** (13-29)†	
Frobin et al.	F: 23-95	**8.4** (3.4)†		**15.2** (4.7)†		**17.0** (5.5)†	
	M: 10-36	**7.8** (3.1)†		**11.6** (3.6)†		**14.4** (4.6)†	
Piché et al.	M+F: 30	**10.5** (4.7)†		**15.6** (5.7)†		**16.1** (6.2)†	

	C5-C6		C6-C7		Ref
author	**ante**	**retro**	**ante**	**retro**	
Van Mam. et al.	**22.6** (18.2-25.4)	**22.6** (18.3-26.0)	**17.1** (15.2-21.7)	**17.8** (16.4-21.5)	[93]
Ordway et al.	**18.6** (2.7)	**9.3** (3.8)	**16.6** (4)	**8.3** (5.8)	[107]
Reitman et al.	/	**15.8** (4.2)	/	**13.5** (5.3)	[126]
Penning et al.	**20** (16-29)†		**15** (5-25)†		[115]
White et al.	**20** (13-29)†		**17** (6-26)†		[154]
Frobin et al.	**17.9** (6.6)†		**11.4** (6.8)†		[39]
	12.20 (5.2)†		**9.8** (5.7)†		
Piché et al.	**15.0** (7.3)†		**14.1** (4.4)†		[118]

versus passive motion, or due to a discrepancies in measurement accuracy: accuracies ranged from 0.76° to 1.9° during flexion and extension (table 1.1).
In addition to these studies, other studies have investigated the effect of age and gender on the IVM. There is a general agreement that women have a greater ROM than men for any given age group [33, 39], and that global ROM decreases with age at a rate of approximately 4° per decade [18, 33, 60].
Bogduk and Mercer suggested that two standard deviations from the mean should be regarded as the normal range [13]. However it might be deceptive to propose a certain range as normal as the intervertebral range of motion is not stable over time. Van Mameren et al. found a difference in intervertebral ROM if the same ten individuals were remeasured after a period of 2 and 10 weeks [94].
Some authors wrongly stated that during flexion, the processes spinous separate in a smooth fan-like progression [13]. This a merely an idealized pattern. In reality the motion of the cervical spine is more complex. Van Mameren et al. revealed a general flexion pattern using lateral cineradiography [93]. Flexion movement is initiated in the lower cervical spine (C5-C7). This initial phase is followed by an increasing contribution of the upper cervical spine. During the final stage, maximum contribution to rotation shifts again to the lower cervical spine.
Intervertebral lateral motion is not restricted to rotation, also AP translation is observed during flexion and extension. A vertebra performs a tilting motion in combination with a sliding motion with respect to the inferior adjacent level. There exists a linear relation between the tilting and sliding [39]. The more caudally located vertebrae primarily show tilting, whereas sliding is distinctly more present in the more cranially located vertebrae [39, 126]. Different possible definitions for AP translation are available. White and Panjabi defined AP translation as the translation of the anterior inferior corner of the superior vertebra with respect to the inferior vertebra [154]. They reported a representative value of 2 mm with a maximum of 2.7 mm. However, in a different study Panjabi et al. found an AP translation of 3.5±0.01 mm in a cadaver study using the same definition [113]. More recently, Reitman et al. measured AP translation as the displacement of the posterior inferior corner of the superior vertebra in the direction defined by the superior endplate of the inferior vertebra [126]. Frobin et al. measured AP translation along an axis coinciding within the midplane of the intervertebral disc [40]. Table 1.3 summarizes the in vivo measured AP translation for each intervertebral level. Because of the multitude of definitions, care must be taken when comparing values of AP translation of different studies.
The center of rotation (COR) qualitatively characterizes motion of the cervical spine. A COR contains information on the rotary as well as the translatory component between two vertebrae of a FSU. Penning was the first to publish

the different locations of the CORs for different cervical segments during flexion/extension [114]. He displayed the CORs graphically but provided no normalization for the mean location of the CORs (figure 1.2).

Table 1.3: In vivo lateral AP translation divided by the mean width of the caudal vertebra(Frobin et al.) or divided by the width of the superior endplate of the inferior vertebra (Reitman et al.)

author	**number**	**C2-C3**	**C3-C4**	**C4-C5**
Reitman et al.	M+F:140	0.117 (0.055)	0.151 (0.051)	0.162 (0.056)
Frobin et al.	M: 28-95	0.181 (0.056)	0.340 (0.070)	0.295 (0.065)
	F: 10-35	0.176 (0.079)	0.302 (0.069)	0.268 (0.065)

author	**C5-C6**	**C6-C7**	**ref**
Reitman et al.	0.117 (0.051)	0.062 (0.039)	[126]
Frobin et al.	0.230 (0.059)	0.140 (0.048)	[40]
	0.229 (0.066)	0.139 (0.072)	

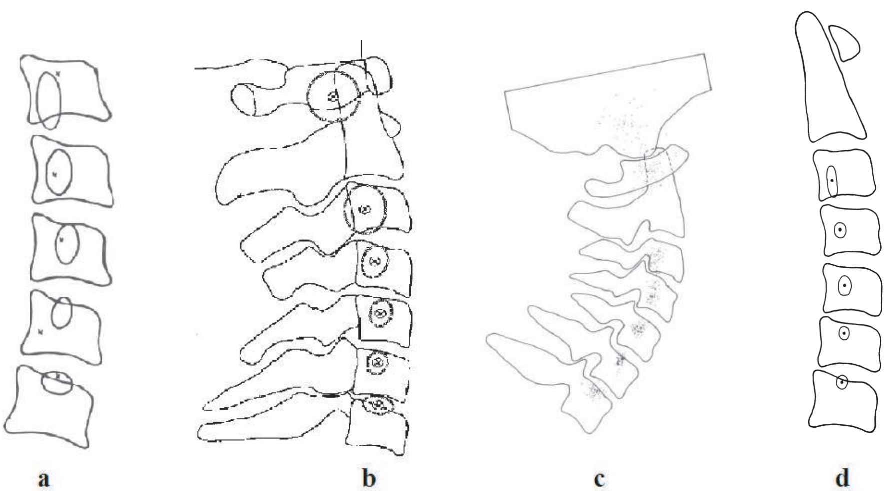

Figure 1.2: Schematic drawings of a lateral view of the cervical vertebral bodies illustrating the location of the center of rotation (COR) for each spinal unit during flexion/extension. a) Location of the mean COR with two standard deviations according to Amevo et al. [4], b) Location of the mean COR with two standard deviations according to Dvorak et al. [34], c) Scatterplot of averaged CORs according to Van Mameren et al. [150], d) Location of the mean COR with two standard deviations according to Bogduk et al. [13]

Amevo et al. [5], Dvorak et al. [34] and Van Mameren et al. [150] developed accurate maps of the location of the CORs during flexion/extension (figure 1.2). The locations of the CORs at lower cervical levels are situated close to the intervertebral disc and close to the middle of the superior endplate. For higher cervical levels, the location of the COR moves more caudally and posteriorly. In contrast to the range of motion the locations of COR are independent of whether they were calculated based on anteflexion or retroflexion sequences; and CORs are remarkably stable over time [13].
Motion in one plane at the cervical spine requires the contribution of complementary motion from individual vertebrae in other planes [13, 94, 116], therefore, lateral bending and axial rotation should be investigated as well. Lateral bending and axial rotation at intervertebral levels are measured with difficulty using radioscopy. MRI, biplanar radioscopy and RSA do provide the possibility to measure these three-dimensional motion patterns as mentioned in 1.3.2.
Due to the anatomy of the facet joints, pure axial rotation or pure lateral bending is not possible in the cervical spine [13]. Any amount of rotation or translation that is consistently associated with rotation or translation about another main axis is called coupled spinal motion [154]. Cook et al. presented an overview of the coupling behavior of the cervical spine [19]. The general conclusion of this review was that axial rotation occurs simultaneously to the same side under lateral bending at levels C2-C3 and caudal and visa versa. Iai et al. and Mimura et al. used biplanar radiography to measure the intervertebral coupling due to axial rotation [100]. Ishii et al. proposed MRI to measure the coupled movement during lateral bending and axial rotation [64, 65]. Table 1.4 summarizes the results of these studies.
Due to the saddle shape of the cervical uncovertebral joints [13], the COR is located superiorly with respect to the intervertebral disc of a FSU during lateral bending (figure 1.3) in contrast to inferiorly with respect to the intervertebral disc of a FSU during flexion/extension (figure 1.2). This discrepancy is of much debate for the design and development process of lumbar and cervical constrained intervertebral disc prostheses [61, 104, 129, 132]. Currently, most ball-and-socket or ball-and-trough devices, such as the Porous Coated Motion (CerviTech) and the Prodisc-C (Synthes), have the ball pointing upward to imitate the inferiorly located COR during flexion/extension; other ball-and-socket devices, such as the Prestige LP (Medtronic), have the ball pointing downward to imitate the superiorly located COR during lateral bending. In a theoretical ideal situation, the position of the center of rotation during both flexion/extension and during lateral bending should be located close the normal in vivo position. Mobile-core or non-constrained prostheses, such as the the Bryan Cervical Disc prosthesis (Medtronic) and saddle-shaped prostheses, such as the Altia TDI (Amedica) and CerviCore (Stryker), provide this possibility.

Table 1.4: Axial rotation (AR) with coupled lateral bending (LB) and flexion/extension (FL/EX). Coupled lateral bending (+) represents same direction of axial rotation. Coupled flexion/extension (+) represents flexion. Results are presented in degrees (SD)

Author		**C2-C3**			**C3-C4**			**C4-C5**	
	AR	**LB**	**FL/EX**	**AR**	**LB**	**FL/EX**	**AR**	**LB**	**FL/EX**
Iai et al.	**3.75**	0.25	-0.21	**3.12**	7.00	-4.00	**3.12**	4.50	0.42
Mimura et al.	**3.7**	1.6 (7.7)	-0.2 (2.7)	**2.9**	6.2 (7.1)	-2.9 (4.7)	**2.1**	6.2 (7.1)	2.1 (4.3)
Ishii et al.	**2.2 (0.9)**	3.6 (1.5)	-1.4 (1.2)	**4.5 (1.1)**	5.4 (1.3)	-2.3 (1.7)	**4.6 (1.1)**	5.0 (1.3)	-1.5 (1.9)

Author		**C5-C6**			**C6-C7**		**Modality**	**Ref**
	AR	**LB**	**FL/EX**	**AR**	**LB**	**FL/EX**		
Iai et al.	**2.50**	4.00	0.63	**2.50**	2.50	1.25	Biplanar radioscopy	[63]
Mimura et al.	**2.7**	4.0 (1.1)	2.1 (3.3)	**3.2**	2.7 (6.5)	2.5 (2.9)	Biplanar radioscopy	[100]
Ishii et al.	**4.0 (1.1)**	5.3 (1.3)	0.9 (1.7)	**1.6 (0.8)**	4.9 (2.1)	2.4 (1.5)	3D MRI	[65]

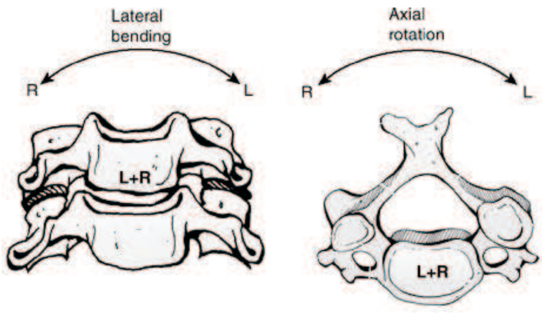

Figure 1.3: Schematic drawings of a frontal and axial view of a cervical spinal unit illustrating the location of the center of rotation (COR) during lateral bending and axial rotation. Adapted from White et al. [154]

None of the aforementioned studies have investigated continuous intervertebral motion patterns during lateral bending and axial rotation, but limited themselves to the assessment of the amount of motion between left and right lateral bending and between left and right axial rotation. Nevertheless, the identification of these continuous motion patterns might provide further insight in the kinematic behavior of the cervical spine and can be used as input for the development of arthroplasty devices as well as to determine whether or not it make sense to use such device.

Intervertebral motion following implantation of an artificial disc

Several authors provided a comparison between preoperative and postoperative lateral ROM [119, 31, 131, 130]. The results of these in vivo radiographic studies suggest that an intervertebral disc prosthesis maintains motion up to 24 months postoperatively. Nevertheless, it would be wrong to state that arthroplasty

Table 1.5: Lateral intervertebral ROM of normal, degenerative, fused and disc-replaced cervical spines. All subjects having a degenerative, fused or replaced disc were symptomatic at C5-C6. Adapted from Goffin et al. [51]. Results are presented in degrees. No standard deviations were available.

Status	Number	C2-C3	C3-C4	C4-C5	C5-C6	C6-C7
normal	M+F: 10	6.7	13.6	20.8	15.1	10.1
disc replaced	M+F: 10	7.7	12.9	15.5	10.9	9.8
degenerative	M+F: 10	6.4	10.2	8.6	7.6	2.6
fused	M+F: 10	9.2	10.2	12.8	0.6	1.1

restores motion to normal, physiological motion. The ranges of motion of these studies were compared to the ROM of symptomatic patients suffering from cervical spondylosis with radiculopathy and/or myelopathy. These patients do not represent asymptomatic individuals and might not exhibit normal ROMs. Goffin et al. presented a study comparing kinematics of normal, degenerative, fused and disc-replaced (with a Bryan Cervical Disc Prosthesis) cervical spines [51]. All subjects having a degenerative, fused or cervical disc replacement were symptomatic at C5-C6. The mean intervertebral ROMs of the groups are summarized in table 1.5. From these results the following conclusions were drawn: Patients having a disc replacement showed the most similar ROMs compared to normal individuals; and patients with a degenerative disc exhibited hypomobility at all levels. The hypothesis that patients with fusion tend to overcompensate the loss of motion in the adjacent levels was however not substantiated in this study.
One study compared the centers of rotation preoperatively and postoperatively after implantation of an intervertebral disc prosthesis. The authors reported that the COR at the level of surgery and at the adjacent levels was preserved following implantation of the Bryan Cervical Disc Prosthesis [119]. They hypothesized that when the location of the COR is preserved, the facets and ligaments are not subjected to abnormal stresses. This result was confirmed by a study using a finite element model [43].
Despite the aforementioned studies, further research is needed whether or not the maintained motion after cervical arthroplasty is physiological and normal both in quantity as well as in quality. Moreover, the influence of postoperative motion on general clinical outcome has not been studied up to date.

1.3.4 Conclusion

The in vivo kinematics of the cervical spine have been numerously studied in the lateral plane. Normal databases for the intervertebral range of motion, anteroposterior translations and centers of rotation have been established. However, several questions regarding cervical motion patterns still need to answered. First, despite the multitude of data on lateral cervical motion patterns, continuous angular motion and continuous translational motion during flexion/extension has been rarely studied. Furthermore, little data is available on three-dimensional continuous intervertebral motion besides flexion/extension, such as lateral bending and axial rotation. Additionally, the influence of intervertebral disc degeneration on invertebral motion has not been studied. Next, it remains unknown whether the maintained motion after cervical arthroplasty is physiological and normal both in quantity as well as in quality. Finally, the influence of postoperative intervertebral motion on clinical outcome still needs to be studied.

1.4 Biomechanics of the middle and lower cervical spine

1.4.1 Introduction

The mechanical behavior of the human cervical spine is quantified by its physical properties. These properties include the geometric, inertial and mechanical characteristics of the complete cervical spine, of functional spinal units (FSU) and of individual components [26].
The mechanical behavior of the human cervical spine can be characterized using a multitude of parameters and coefficients. Load-displacement curves are frequently used. From these curves, the neutral zone (NZ), the elastic zone (EZ), the range of motion (ROM) and the flexibility or stiffness coefficients can be calculated. Figure 1.4 shows a typical load displacement curve with definitions of the different parameters. Other parameters that describe the biomechanical behavior of the cervical spine are e.g. the stresses and strains in the intervertebral disc [96], the contact forces in the facet joints [80], and intradiscal pressure [121, 152].

1.4.2 Measuring and assessment techniques

It is not straightforward to measure the human biomechanics of the cervical spine in vivo. Because invasive techniques such as measuring intradiscal pressure and inducing specific injuries are ethically not acceptable, only a few studies were published using an in vivo human model [99, 96].
Next to in vivo biomechanical models there is a large amount of other models available: physical models, in vivo animal models, in vitro models and computer models. These models can provide insight into the external and internal biomechanics of the cervical spine.

Physical biomechanical models

In physical models the vertebrae are represented by artificial materials. This model can be used if bony anatomy and physical properties of soft tissues are less important [111]. Many of the test protocols in the ASTM standards

(F1717-04, F2346-05) rely on this type of biomechanical models.
Brodke et al. used a physical model to evaluate the load-sharing properties and to measure the stiffness of dynamical cervical plates [14].

In vivo animal models

Although the anatomy of the cervical spine can be very different from human cervical spines, in vivo animal models can be used to study the biomechanics of the cervical spine. Similarities in biomechanical behavior between sheep and human spines have been observed [70, 158]. Moreover, in vivo animal models are able to mimic cellular responses occurring in the cervical spine and can therefore be used to investigate wear debris and bone ingrowth after disc replacement surgery.
Anderson et al. used a caprine and chimpanzee model to investigate wear debris and to assess the inflammatory response after implantation of a Bryan Cervical Disc Prosthesis (Medtronic, Memphis, USA) [8, 9]. Wear debris was

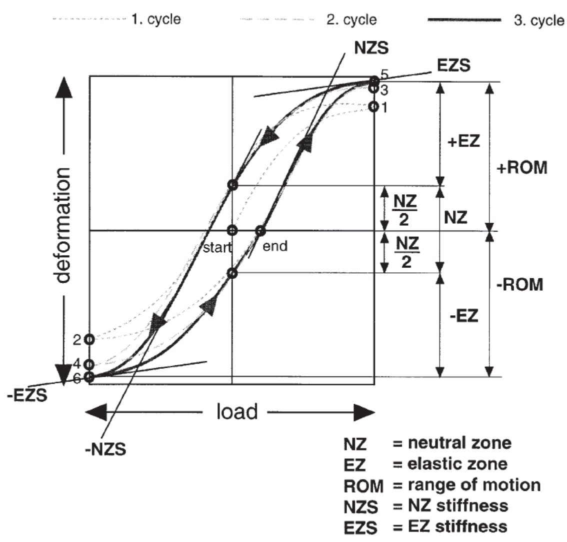

Figure 1.4: Load-displacement curve of single functional spinal unit with definitions of the parameters (neutral zone: NZ, elastic zone: EZ, range of motion: ROM, neutral zone stiffness: NZS, elastic zone stiffness: EZS) [160]

found in periprosthetic tissues and polymeric debris was observed in loose connective tissue in the epidural space. No inflammatory responses were observed. Jensen et al. reported 30.1% bone ingrowth (min. 17.7%-max. 37.0%) three months after implantation of a Bryan Cervical Disc Prosthesis in two chimpanzees [68]. McAfee et al. observed no cellular reaction and no granular tissue response to any particular wear debris in a caprine model, six months after implantation with a Porous Coated Motion (PCM) Prosthesis (Cervitech, Roundhill, USA) [98].

In vitro models

In vitro cadaveric models are most commonly used to assess the general biomechanics of the human cervical spine [111].
Two main different approaches of applying quasi-static loads or motion exist in cadaveric studies: the stiffness method and the flexibility method. Other approaches such as the hybrid protocol are more recent developments.

- The stiffness method (or motion control) applies an amount of motion in a particular direction, while measuring the resulting loads.
  Fuller et al. used this method to evaluate the distribution of motion across adjacent segment after a segmental arthrodesis in the cervical spine [41]. They found that the compensation in motion due to fusion was evenly distributed over all segments cranially and caudally with respect to the treated level. In contrast, using a similar technique Schwab et al. reported an increase in motion at segments immediately adjacent to a single-level fusion in the cervical spine [133].

- The flexibility method (or load control) is most widely used in cadaveric testing. Often a pure moment is applied on the superior vertebra and the resulting unconstrained motion is measured. Although pure moment loading does not represent loading in real life due to its reduced complexity [1], it is an attractive technique. The use of non-constraining pure moments ensures that the load experienced by a specimen remains constant along its length independent of its geometry, stiffness or motion [21, 90, 110]. Wilke et al. reported that the application of pure moments in vitro to intact lumbar spinal segments produced loads comparable with loads observed in vivo [159]. However, they also reported that removing a disc or a vertebra led to inconsistent implant loads in an in vitro experiment.
  Different designs of non-constraining pure moment loading apparatuses have been published [21, 90, 112]. Recent studies used a computer

controlled six-degree of freedom spinal simulator to apply pure moments about each axis [23, 157, 159].

- A hybrid protocol applies the same overall motion for the intact specimen as well as for the instrumented construct by applying pure moments [28, 46]. The global range of motion of the intact specimens is measured following the flexibility protocol. Next, pure moments are applied to the instrumented specimen until identical global motion is achieved. Goel et al. claimed that the hybrid protocol better reproduced clinical observations in terms of motion after surgery [45].

Up to date in vitro experiments have established a very detailed description of the biomechanics of the intact cervical spine. Panjabi et al. provided detailed intersegmental NZ and ROM values together with load-displacement curves for every cervical FSU using a multidirectional flexibility testing protocol [112]. Wheeldon et al. proposed a statistical description of the load-displacement curves by a nonlinear logarithmic function $\theta = A\ ln(B \cdot M + 1)$, where θ is the angular rotation ($^{\circ}$) and M is the applied moment (Nm) [153]. They provided the model constants A and B. Cripton et al. proposed a minimally disruptive technique for measuring intervertebral disc pressure in the cervical spine [22]. They found a 2.4 to 3.5 MPa peak pressure under a compression force of 800 N. They assumed hydrostatic pressure in the nucleus pulposus. Pospiech et al. established normal values for intradiscal pressure and load-pressure curves under physiological condition for C3-C4 and C5-C6 [121]. A pure flexion/extension moment generated an intradiscal pressure of 0.32 (0.12 - 0.43) MPa at C3-C4 and of 0.23 (0 - 0.56) MPa at C5-C6.

Furthermore, cervical spines with an intervertebral disc prosthesis or interbody fusion have been numerously studied in vitro. Wigfield et al. compared internal stress distributions in cervical intervertebral disc for intact specimens, specimens with an artificial disc (Bristol Disc, Medtronic, Memphis, USA) inserted and specimens with simulated fusion [156]. Fusion resulted in significant increases in peak stresses within the annulus fibrosus of each adjacent disc compared to intact specimens and specimens implanted with an intervertebral disc prosthesis. No difference in mean stress between the groups was observed. In a similar study, Dmitriev et al. found no differences in NZ and ROM at the operated level and intradiscal pressure at adjacent levels between the intact and the cervical disc replacement group (PCM, Cervitech Inc., NJ) [28]. They reported a 31% increase in the adjacent level ROM both for the fusion groups, and a 21% increase for the group with the cervical disc prosthesis compared to intact specimens. However, no significant difference was found.

Using a dynamic axial impulse test and an axial cyclic loading test, Dahl et al. compared the dynamic characteristics of intact, fused and prosthetic-replaced

(Bryan Cervical Disc Prosthesis) cervical discs in cadaveric specimens [24]. They found that fusion significantly increased the dynamic stiffness compared to the intact and implanted specimens. Next, they observed that implanted constructs absorbed significantly -by an order of a magnitude- more energy and showed a increased viscous damping ratio of respectively 11% and 26% (though not significant) compared to intact and fused constructs. From these results they concluded that a prosthetic cervical disc is a more dynamically biofidelic alternative to intervertebral fusion.

General observations of in vitro cadaver experiments investigating the biomechanics and kinematics of the cervical spine were that an intervertebral disc prosthesis can replicate physiologic motion at the affected and adjacent levels [23, 27, 28, 98, 122] and cervical fusion introduced an increased intervertebral motion and intradiscal pressure at adjacent segments [28, 35, 121, 124, 133]. However, up till now, a perfect placement of the prosthesis was assumed when investigating the influence of cervical arthroplasty on the biomechanics of the cervical spine. Manufactures consider it to be important that the prosthesis is placed according to their guidelines, as perfect placement would be imperative for a good functionality of the prosthesis [55, 105].

Computer models

A computer model is a set of mathematical equations that incorporate the geometry and physical properties of the structure they represent [111]. A finite element model (FEM) is the most commonly used computer model. FE analyzes and in vitro cadaveric testing are complementary techniques; neither can provide a complete picture of the biomechanics of the cervical spine [45]. Studies of kinematics, biomechanics and -in contrast to in vivo and in vitro measurements- also internal strains and stresses are possible study subjects of FE analyzes [111, 164]. Moreover, FEM has been coupled with adaptive bone remodeling to investigate for example the temporal changes associated with fusion devices [46]. However, any mathematical model must be validated with experimental data to provide realistic estimations of the internal and external responses of the soft and hard tissues of the cervical spine [164]. Care must be taken when extrapolating results from the validated model.

According to Yoganandan et al. a FEM should accurately represent the cervical spine in the following aspects: anatomy, material properties of the spinal components, boundary and loading conditions and a FEM should be validated against experimental data [165]. They provided a historical overview of the development of FEMs and its clinical applicability. More recently, the same authors provided a very detailed overview of the role and the biomechanical parameters (material en geometric properties) of the soft tissues used in FEMs [164]. Up to date, detailed, three-dimensional nonlinear

Table 1.6: Details of the in vitro cadaver experiments. NR: not reported. †Only flexion/extension. ‡ MFS: Muscle force simulation. *IDP: Intradiscal pressure

Author	**Nr**	**Levels**	**Status**	**Protocol**	**Magnitudes**
Miura et al.	6	C2-T1	Intact	Flexibility+preload	1:1:1 versus 2:2:4 Nm + 100 N
Panjabi et al.	16	C0-C7	Intact	Flexibility	1:1:1 Nm
Wheeldon et al.	7	C2-C1	Intact	Flexibility	2 Nm†
Pospiech et al.	7	C2-C7	Intact vs fusion	Flexibility+MFS‡	0.5:0.5:0.5 Nm
Richter et al.	6	C4-C7	Intact vs injured	Flexibility	2.5:2.5:2.5 Nm
Eck et al.	6	C3-T1	Intact vs fusion	Stiffness	20° FLX 15° EXT
Wigfield et al.	9	C2-T1	Intact vs fusion vs prosthesis	Stiffness	15° FLX 10° EXT 10° LB
Dmitriev et al.	10	C3-T1	Intact vs fusion vs prosthesis	Hybrid	5:5:5 Nm
McAfee et al.	7	C3-C7	Intact vs fusion vs prosthesis	Flexibility+preload	NR
DiAngelo et al.	4	C2-T1	Intact vs fusion vs prosthesis	Stiffness	NR
Puttlitz et al.	6	C2-C7	Intact vs prosthesis	Flexibility+preload	1:1:1 Nm + 22 N
Dahl et al.	5	C4-C7	Intact vs fusion vs prosthesis	Dynamic Impulse; Cyclic loading + preload	400 N impulse; 0.25 mm sinus + 52 N

Author	**Motion tracking**	**Accuracies**		**IDP***	**Ref**
Miura et al.	Optotrack	0.014°	NR	No	[101]
Panjabi et al.	Stereophotographs	0.17°-0.60°	0.22-0.43 mm	No	[112]
Wheeldon et al.	Motion Capture System	0.1°	0.2 mm	No	[153]
Pospiech et al.	/	/	/	Yes	[121]
Richter et al.	Zebris	0.2°	NR	No	[127]
Eck et al.	Motion analysis system	NR	NR	Yes	[35]
Wigfield et al.	/	/	/	Yes	[156]
Dmitriev et al.	Optotrack	NR	NR	Yes	[28]
McAfee et al.	Optotrack	NR	NR	No	[98]
DiAngelo et al.	Joint Motion Tracker	0.2°	0.112 mm	No	[27]
Puttlitz et al.	Motion Capture System	0.1°	NR	No	[122]
Dahl et al.	Motion analysis system	/	5 μm	No	[24]

viscoelastic finite element models of the human cervical spine have been developed [15, 43, 56, 146]. Yoganandan et al. provided an excellent overview of the finite element models developed up to 1995 [165]. Table 1.7 provides an overview of the more recent FE studies.

Multiple finite element models have been developed to study the biomechanics of intact cervical spines. Some authors observed that variation in hard tissue structures (e.g. cancellus core, cortical shell) had little influence on the external and internal responses of the cervical spine in contrast to the material properties of the soft tissues (e.g. intervertebral disc, ligament structures) which had a preponderant influence [15, 78]. Kumaresan et al. observed that the ventral region of the intervertebral disc resisted higher variations in axial force while the dorsal region transmitted higher shear forces under flexion or extension in addition to a compression force [79]. These region specific forces formed a basis to explain the local appearance of osteophytes spanning the anterior body-disc medium and disc herniations [164].
Many researchers evaluated intervertebral disc prostheses in the lumbar spine using finite element models [29, 45, 46]. But because of characteristic differences, a direct comparison/extrapolation from the lumbar to the cervical spine should not be made [164]. Nevertheless, some FE studies on cervical arthroplasty exist. Ha et al. showed that fusion reduced the mobility of the treated level by 50-70%. In contrast, an elastomeric artificial disc prosthesis with a Young's modulus of 5.9 MPa restored the biomechanical behavior (ROM, facet contact forces and ligament forces) of the intact spine. Galbusera et al. found that the load-displacement curves of the model with incorporation of an artificial disc (Bryan Cervical Disc Prosthesis) were comparable to the curves from the intact model; an increase in stiffness was however observed in the model with the prosthesis [43]. They calculated the CORs and found a qualitative match with the CORs of the intact model.
To summarize, FEMs of the cervical spine have been used to e.g. investigate the role of the facet joints [77, 161], study the influence of an artificial disc on the biomechanics at the index and the adjacent levels [42, 84, 43, 56, 106, 85], assess the influence of osteophyte formation [80], and compare different implant designs [85, 128, 104]. However, the influence of a possible malplacement of the prosthesis has nog been studied. As mentioned previously, perfect placement might be important for a good functionality of the prosthesis and to obtain good long term clinical results.

Table 1.7: Summary of finite element studies. † Validation of the FEM against in vitro experiments or against results from previously published FE studies.

author	Model	Status	Validation†	Loading	Results	Ref
Yoganandan et al.	3D C4-C6	intact	in vitro [137]	Axial compression	Stresses in vertebral bodies and endplates	[166]
Maurel et al.	3D parameterized C3-C7	Intact	in vitro [103]	Pure moments (2 Nm)	ROM, coupled movement, stiffness coefficient	[97]
Goel et al.	3D C5-C6	intact	in vitro [103]	Axial compression (73.6 N), pure moments (1.8 Nm)	Intradiscal pressure, forces across facets, tension in ligaments	[44]
Kumaresan et al.	3D C4-C6	intact	NR	NR	ROM, disc stress and endplate stress	[78]
Kumaresan et al.	3D C4-C6	intact	in vitro [120]	Axial compression + eccentric loads	Strains, shear forces and intradiscal pressure	[79]
Brolin et al.	3D C0-C3	intact	in vitro [47, 109]	Axial tension (1500 N), pure moments (1.5 Nm)	Load-displacement, ROM, coupled movement	[15]
Teo et al.	3D C4-C6	intact vs resection of soft tissues	in vitro [137] + FEM [166]	Compression (1 mm) + pure moment (1.8 Nm)	Load-displacement	[146]
Kumaresan et al.	3D C4-C6	Intact vs disc degeneration	in vitro [120]	Axial compression (80 N)	Load-displacement, strains and stresses in soft tissues, stiffness, strain energy density	[80]
Ha	3D C3-C6	Intact vs fusion vs prosthesis	in vitro [103] + FEM [146]	Pure moments (1 Nm)	ROM, contact forces	[56]
Galbusera et al.	3D C5-C6	Intact vs prosthesis	in vitro [103] + FEM [146]	Axial compression (73.6 N), pure moments (1.8:1:1 Nm)	Load-displacement, stiffness coefficient, ICR	[43]

1.4.3 Conclusion

In vitro experiments and computer models have been used to describe the biomechanics of the cervical spine in detail. These in vitro and in silico studies showed that intervertebral disc prostheses are able to preserve motion in the cervical spine qualitatively as well as qualitatively and are able to mimic the mechanical as well as dynamical behavior of an invertebral disc. However, the influence of a malplaced prosthesis on the kinematics and kinetics of the cervical spine has not been studied up to date.

1.5 Grading systems for cervical degeneration of intervertebral discs and facet joints

1.5.1 Introduction and background

Cervical spine degenerative disease is a disorder that affects the quality of life in symptomatic patients. Degenerative disease refers to a pathologic change in the normal architecture of the cervical intervertebral discs and facet joints. It has been unclear so far what the initiating events are and what influences progression.

Various pathologic processes may cause degenerative change in the cervical spine [54, 10]. From the clinical perspective, cervical disc or facet joint degeneration is believed to be a source of chronic pain, and over 90% of spine surgical procedures are performed because of consequences of the degenerative process [11, 36]. Linton et al. [88] estimated the prevalence of spinal pain in the general population as 66%, with 44% of the patients reporting pain in the cervical region. Most people with degenerative changes in the cervical spine remain asymptomatic. Symptomatic patients are usually older than 40 years of age with symptoms presented as compression of neural structures. Three main symptom complexes are neck pain, cervical radiculopathy, and cervical myelopathy [67, 88]. The evaluation of the severity of cervical degeneration is important in deciding the operative procedure and treatment level in patients with cervical disc degeneration or degeneration of the facet joints. However, there is no consensus on what 'cervical spine degeneration' actually is or how it should be distinguished from the physiologic processes of growth, aging, healing, and adaptive remodeling.

1.5.2 Cervical intervertebral disc degeneration

Introduction

Disc degeneration can lead to major structural failure or pathological changes. During the pathological development, accurately defining degenerative features will most likely influence the patients' diagnosis and indicate which the best targets are for therapeutic interventions and treatment.
Cervical spine degeneration involves biologic changes in cell-mediated mechanisms, which are most pronounced in the nucleus and gross structural changes, most evident in the annulus and endplate [138, 151]. Disc degeneration begins when catabolism and/or the failure to retain matrix proteins consistently exceed synthesis and/or retention. These anatomic changes lead to decreased flexibility and loss of fluid pressurization. The decreased disc height contributes to changes in the local stress/strain state within the disc directly and painful responses indirectly [6, 141]. The effect of structural changes in the disc on the clinical and biomechanical characteristics of the spinal segment has been investigated for many years [10, 141, 167]. The cervical intervertebral disc is a major component for segmental stability as well as major load-bearing structure [138, 151]. A degenerative disc adversely affects the biomechanical behavior of cervical spine motion segments which leads to secondary pathological changes including narrowing or height loss of intervertebral disc, osteophyte formation on anterior and posterior borders of the vertebral endplates and endplate sclerosis [155]. Disc degeneration also occurs as a natural part of aging. Early degenerative changes would refer to accelerated age-related changes in a structurally intact disc. Structural failure is irreversible because adult discs have only a limited ability to recover from any metabolic or mechanical injury [2, 135, 138].
It is still unclear what degree of degeneration could cause symptoms.Cervical arthroplasty sometimes is the treatment of choice after a diagnosis of cervical disc degeneration. However, it is unknown what extend of disc degeneration should be included as a contraindication when selecting patients for this surgical solution.
An assessment based on imaging to distinguish and quantify normal and degenerative intervertebral discs might therefore be helpful. There are many different systems to grade spinal disc degeneration, but for the cervical spine, such data are rare [71, 53, 52, 50]. The morphological changes during cervical spine degeneration have often been described by many different imaging techniques such as plain radiography [102], discography [142], computed tomography and MRI [147].

Grading systems based on lateral radiographs

Radiographic assessment can be chosen as input for a grading method and has several advantages: in contrast to macroscopic and histological systems, it can also be applied in vivo; in contrast to discographic systems, it is less invasive; and in contrast to grading systems based on magnetic resonance images or computed tomography scans, it requires only a standard X-ray machine and is therefore less expensive [25, 69]. Height loss of the intervertebral disc, osteophyte formation, and endplate sclerosis are defined in pragmatic terms and usually mentioned in the epidemiologic and radiologic literature [71, 123]. According to the review of Kettler et al. [73], four major scoring systems for cervical disc degeneration based on lateral radiographs exists: Kellgren et al. [71], Gore et al. [53], Goffin et al. [50] and Kettler et al [75]. Only the scorings systems of Kellgren et al. and Kettler et al. were tested for reliability. The inter-rater reliability of both scoring systems fulfilled the criterion for recommendation (ICC>0.60) [73]. The scoring systems of Kellgren et al., Gore et al. and Goffin et al. are descriptive and subjective rather than quantifiable. The scoring system of Kettler et al. is objective and quantitative, but complex and cumbersome. They validated their scoring system using lateral radiographs of human cadaveric osseoligamentous spine specimens, and used macroscopic slices of the respective cadaveric specimens to assess the 'real' degree of degeneration. They found that the 'real' degree of disc degeneration was underestimated in 64% of all discs [75].

1.5.3 Cervical facet joint degeneration

Introduction

The facet or apophysial joints are one of the main structures for the stability of the spinal motion segment [57, 74]. Facet joints are clinically important spinal pain generators that have been shown to be capable of causing neck pain in a significant proportion of patients [74, 76]. Recently, clinical and pathologic investigations have targeted the facet joints as possible sources of pain in patients with cervical degeneration [89, 148].
Degeneration of facet joints is diagnosed if sclerosis, osteophyte and hypertrophy of these joints are detected [163]. Facet joints are true synovial articulations and undergo degenerative changes identical to those of osteoarthritis seen in other synovial joints [82]. Major trauma or repetitive minor trauma may lead to a nonspecific synovitis. Gradually, the hyaline cartilage that lines the joint loses its water content. Eventually, the cartilage wears completely away [76, 89]. The cervical articular processes begin to slide over each other

as the joint capsules become stretched. This results in a malalignment of the facet joints and abnormal biomechanical function of the motion segment. As a result, a hypertrophic process on the articular surfaces and narrowed joint space between superior and inferior articular process may develop. There can be various degrees of cervical facet joint degeneration in the same patient.

Grading systems for degeneration of facet joints

Degeneration of cervical facet joints has been graded rarely. Some grading systems were based on the macroscopic anatomy, e.g. Silberstein et al. [140], and plain radiography, e.g. Kellgren et al. [72]. No systems using computed tomography or magnetic resonance imaging were found in the literature. Cote et al. [20] pointed out that Kellgren's classification system for apophysial joint degeneration did not have the level of reliability necessary to be used in outcomes research. Moreover, it did not fulfill Kettler et al.'s criteria for recommendation (ICC>0.40) [73]. Computed tomography scans might improve the visibility and therefore early degenerative changes of the facet joints might be better detected.

1.5.4 Conclusion

The process of cervical disc degeneration and facet joint degeneration is explained. Based on the current review of scoring systems for intervertebral disc and facet joint degeneration, a quantitative and non time consuming scoring systems for cervical disc degeneration based on lateral radiographs and a quantitative scoring system based on CT scans for facet joint degeneration is needed.

1.6 Conclusion

In this chapter the conventions that are used throughout this thesis were discussed. Moreover studies on the kinematics and biomechanics of the cervical spine of healthy individuals and of patients with an intervertebral disc prosthesis were summarized. Finally, the process of cervical disc degeneration and facet joint degeneration was explained.
From this literature review, it can be concluded that despite the large amount of data available on the kinematics and biomechanics of the cervical spine, literature still has important voids that need to be filled:

- Continuous angular motion and continuous translational motion during flexion/extension have been rarely studied.
- No data is available on three-dimensional continuous intervertebral motion besides flexion/extension, such as lateral bending and axial rotation.
- The influence of intervertebral disc degeneration on invertebral motion has not been studied in depth.
- The importance of postoperative intervertebral motion on clinical outcome is still under investigation.

In vitro and in silico studies have been used to describe the biomechanics of the cervical spine in detail, however:

- The influence of a malplaced prosthesis on the kinematics and kinetics of the cervical spine still needs to be investigated.

The process of cervical disc degeneration and facet joint degeneration is explained. Based on the current review of scoring systems for intervertebral disc and facet joint degeneration,

- A quantitative and qualitative, non time consuming scoring system for cervical disc degeneration based on lateral radiographs and a precise scoring system based on CT scans or MRI scans for facet joint degeneration is required.

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Chapter 2

Research questions

The previous chapter has introduced cervical arthroplasty as a multidisciplinary research domain that involves state of the art developments for patients who need an operation for degenerative disc disease. This multidisciplinary approach was also followed in this research and will become clear in this chapter when elucidating the aim and outline of the thesis. The different specific objectives are stated. These objectives together are the base for the underlying hypotheses of this thesis.

2.1 Objectives

- Before cervical intervertebral motion patterns can be analyzed, an appropriate motion tool has to be developed and validated. This is **first objective** of this thesis and is the scope of chapter 3. Such a tool has to be as accurate as the current gold standard. But in addition to the existing tools, the tool should be fast to enable usability in clinical practice and to assure repeatability, it should be preferably user independent.

- The **second objective** and aim of chapter 4 is to develop and validate scoring or grading systems for cervical disc and facet joint degeneration. These scoring systems have to be quantitative, accurate, repeatable. Moreover, the scoring systems should be discipline and experience independent in order increase the number of potential users.

- Many databases of full flexion and extension motion patterns exist. However, there is a need for information on cervical motion besides flexion and extension, and on *how* the cervical spine moves next to *how much* it moves. Using the aforementioned motion tool and scoring systems, the **third objective** is to put together a database of continuous motion patterns of volunteers of different ages with different degrees of disc degeneration. These motion patterns are obtained from lateral and anteroposterior fluoroscopic cameras. From these image sequences, intervertebral motion patterns in the different planes, such as flexion/extension, lateral bending and axial rotation, are calculated. In addition to these motion patterns, also degeneration of the intervertebral discs is assessed in order to correlate the degree of degeneration with motion of the cervical spine. This objective is addressed in chapter 5.

- In chapter 6, the **fourth objective** is addressed. The influence of preoperative intervertebral motion and disc degeneration on postoperative motion, postoperative adjacent level disc degeneration and clinical outcome is assessed in a prospective long term study of patients operated with a Bryan Cervical Disc prosthesis at one level.

- The **fifth objective** is to determine whether or not intervertebral disc prostheses restore motion patterns that are typically found in healthy subjects of the same age, both in quantity as in quality. The goal is to investigate lateral continuous intervertebral motion patterns of patients with a cervical disc prosthesis and to compare them to the database of motion patterns of healthy individuals. This objective is addressed in chapter 7.

- The **sixth objective** is to analyze the influence of a change in surgical technique and a change in patient selection criteria on radiographic outcome. In chapter 8, postoperative segmental alignment is investigated in a retrospective radiographic analysis of two cohorts of patients operated with a Bryan Cervical Disc prosthesis. The surgical technique and selection criteria was changed between both groups.
- The **seventh** and final **objective** is to study the impact of prosthesis malplacements to determine the surgical accuracy which is needed to obtain biomechanical and clinical acceptable results. In vivo postoperative implant positions are assessed in a retrospective radiographic analysis. Next, a finite element model is used to determine the influence of these prosthesis malplacements on the biomechanics of the index and adjacent levels. The results of this investigation are reported in chapter 9.

2.2 General hypothesis

The ultimate goal of cervical arthroplasty is to achieve good clinical outcome, excellent patients satisfaction and proper implant function on the long run while maintaining or even to restore mobility at the operated level. The first underlying hypothesis of this thesis is that proper patient selection in terms of preoperative mobility at the index level, the absence of pre-existing intervertebral disc degeneration at the index level and lordotic preoperative segmental alignment is imperative for long term postoperative mobility and proper alignment after surgery. The first six objective will try to substantiate this hypothesis. The second hypothesis is that, to guarantee long term functioning of the prosthesis and clinical outcome, accurate implant positioning is essential. The sixth and seventh objectives of this thesis have to confirm this statement.

2.3 Technical objectives

In paragraph 2.1 several objectives were listed that are needed for the confirmation of the hypotheses stated in paragraph 2.2. However, some of these objectives require the solution of a technical problem or the use of existing engineering techniques. The paragraphs below provide a brief overview of some of the specific technical objectives of this thesis that were not listed in paragraph 2.1.

2.3.1 Calculation of intervertebral motion patterns

The first objectives of this thesis is to develop and validate a motion analysis algorithm to calculate intervertebral motion patterns based on lateral radiographs or fluoroscopy. The algorithm should ideally be user-independent and on-the-spot useable. To meet these criteria, the algorithm that is developed and validated in this thesis will consist of two steps. In a first step, a feature of the object that needs to be traced should be identified on the radiographs or fluoroscopic image sequence. For the algorithm in this thesis, the cervical vertebrae are chosen as objects and the contours of the vertebral bodies act as features.

Therefore, the contours of each vertebral body v have to be segmented in every frame i of the image sequence, with a total of N frames. This will yield $\mathbf{C_{v,i}}$, i.e. the contour of vertebra v in frame i.

There are several techniques to identify vertebral contours, manual pinpointing being most commonly used (cfr. 1.3.2). However, to meet the criterion of user-independency, an automated segmentation method is called for. Such a method is developed during this thesis in collaboration with the Center for Processing Speech and Images (KULeuven, Beligum). This method requires prior knowledge on the shape S and gray-level appearance GL of the contours of the vertebral bodies. Minimizing a weighing function f yields the contours of each vertebra v in frame i:

$$\mathbf{C_{v,i}} = \min f(S, GL) = (\mathbf{X_{v,i}}, \mathbf{Y_{v,i}}),\ \forall\ v = 2:7, \forall\ i = 1:N, \tag{2.1}$$

In this equation $\mathbf{X_{v,i}}$ and $\mathbf{Y_{v,i}}$ are two vectors of p consecutive points of the contour in the image coordinate system.

In a second step, the features are used to calculate the planar displacements, in terms of a rotation and translation, of the objects they represent. It is assumed that the features are not deformed during imaging. In this thesis, the assumption is valid as the vertebral bodies do not deform during motion and out-of-plane motion can be minimized with proper patient or volunteer coaching. To calculate intervertebral motion, the contour of a vertebra v has to be matched to the contour of that vertebra in an arbitrary reference frame q. The matching technique that is used in this thesis is the iterative closest point (ICP) algorithm. This algorithm minimizes the overall distance $E_{v,i}$ between $\mathbf{C_{v,i}}$ and $\mathbf{C_{v,q}}$ to yield $\mathbf{R}(\alpha(\mathbf{v}, \mathbf{i}), \mathbf{t_{v,i}})$, the planar transformation matrix with respect to the reference frame q.

The planar transformation matrix provides the planar rotation $\alpha(v, i)$ and translation $\mathbf{t_{v,i}}$ of vertebra v in frame i with respect to frame q in the image coordinate system. The ICP algorithm is chosen to match the features as is does not require corresponding points of $\mathbf{C_{v,i}}$ and $\mathbf{C_{v,q}}$. However, ICP is

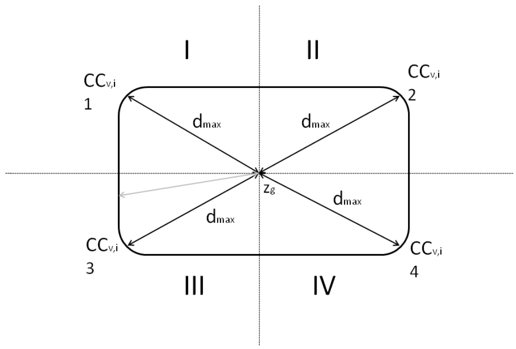

Figure 2.1: Four corners on a vertebral contour. The corners are defined as the points on the contour in quadrant I, II, III and IV, which have the largest distance with respect to the geometric center of the contour

monotonically convergent, i.e. it always converges to a local minimum. To ensure convergence to the global minimum, good initialization is required. In this thesis, a weighted least square method was implemented as robust preconditioner for the ICP. In this preconditioning step, the following weighted equation is minimized:

$$\mathbf{A}^T \cdot \mathbf{W} \cdot \mathbf{A} = 0 \tag{2.2}$$

$$\mathbf{A} = \mathbf{R}(\alpha(v,i), \mathbf{t_{v,i}}) \cdot \mathbf{CC_{v,i}} - \mathbf{CC_{v,q}} \tag{2.3}$$

In this equation, $\mathbf{CC_{v,i}}$ and $\mathbf{CC_{v,q}}$ contain the coordinates of the four corners of the vertebral bodies represented by $\mathbf{C_{v,i}}$ and $\mathbf{C_{v,q}}$. Those corners are defined as the points on the contour in quadrants I, II, III and IV, which have the largest distance with respect to the geometric center z_g of the contour $\mathbf{CC_v}$ in frame i and q, as in figure 2.1. $\mathbf{W}$ is a diagonal matrix with weights for each corresponding point of $\mathbf{CC_{v,q}}$ and $\mathbf{CC_{v,i}}$.
In this thesis, the output of the matching step is used to calculate physiological parameters such as intervertebral rotation $\alpha"(v, v+1, i)$, anteroposterior translation $t_x"(v, v+1, i)$ and craniocaudal translation $t_y"(v, v+1, i)$ between vertebrae $v+1$ and v in frame i with respect to frame q.

$$\mathbf{C'_{v,q}} = \mathbf{R}(\alpha(v,i), \mathbf{t_{v,i}}) \cdot \mathbf{C_{v,i}} \tag{2.4}$$

$$\mathbf{C'_{v+1,q}} = \mathbf{R}(\alpha(v+1,i), \mathbf{t_{v,i}}) \cdot \mathbf{C_{v+1,i}} \tag{2.5}$$

$$
\begin{aligned}
&\mathbf{R}(v, v+1, i) \\
&\quad = \mathbf{R}(\alpha(v,i), \mathbf{t_{v,i}})^T \cdot \mathbf{R}(\alpha(v,i), \mathbf{t_{v,i}}) \qquad (2.6) \\
&\quad = \begin{pmatrix} \cos\alpha\text{"}(v, v+1, i) & \sin\alpha\text{"}(v, v+1, i) & t_x\text{"}(v, v+1, i) \\ -\sin\alpha\text{"}(v, v+1, i) & \cos\alpha\text{"}(v, v+1, i) & t_y\text{"}(v, v+1, i) \\ 0 & 0 & 1 \end{pmatrix} (2.7)
\end{aligned}
$$

where $\mathbf{R}(v, v+1, i)$ is the planar transformation matrix of vertebral v in a coordinate system attached to vertebra $v+1$.
The implementation and validation of such an algorithm is the topic of chapter 3. The validated algorithm than will be used throughout this thesis.

2.3.2 Validation of a scoring system with discrete variables

The second objective is to develop and validate scoring systems for the assessment of intervertebral disc and facet joint degeneration based on lateral radiographs or CT scans. In these scoring systems variables will have to be scored on a numerical interval scale, e.g. from 0 to 5, or ordinal scale, e.g. moderate, good, excellent. The type of scale has important implications on the permissible statistics. For the former, the mean, standard deviation, correlation coefficients and derived statistics may be computed. For the latter, solely the median, percentile and derived statistics should be calculated. For this reason, a numerical scale will be used whenever possible. As discussed in section 1.5, many of the existing scoring systems are descriptive and subjective. A numerical scoring system to score intervertebral disc degeneration and facet joint degeneration, as proposed in this thesis, has the great potential of being quantifiable and allows the calculation of common statistics as described earlier. To validate a scoring system, the consistency or conformity of measurements made by multiple observers, i.e inter-rater agreement, or made by one observer on multiple occasions, i.e. intra-rater agreement, have to assessed. The intraclass correlation coefficient (ICC) is a suitable parameter for such an analysis and is chosen in this thesis. The key difference between the standard Pearson correlation coefficient and an ICC is that in the ICC, the data are centered and scaled using a pooled mean and standard deviation, whereas in the Pearson correlation, each variable is centered and scaled by its own mean and standard deviation. The ICC for multiple groups is caculated as follows:

$$\bar{x} = \frac{1}{KN-1}\sum_{n=1}^{N}\sum_{k=1}^{K}x_{n,k} \tag{2.8}$$

$$s^2 = \frac{1}{KN-1}\sum_{k=1}^{K}\sum_{n=1}^{N}(x_{n,k}-\bar{x})^2 \tag{2.9}$$

$$ICC = \frac{K}{K-1}\frac{N-1\sum_{n=1}^{N}(\overline{x_n}-\overline{x})^2}{s^2} - \frac{1}{K-1} \tag{2.10}$$

where $x_{n,k}$ are paired data values with n=1:N data points for k=1:K groups and $\overline{x_n}$ is the mean of the sample n. As the left term in equation 2.10 is non-negative, the ICC should satisfy

$$ICC > \frac{-1}{K-1} \tag{2.11}$$

Like the correlation coefficients, ICCs are confined to the interval [-1,+1].
The ICC is used in chapter 4 during the validation of the scoring systems. The numerical scoring systems that are proposed in this thesis have the advantage of being quantifiable compared to the subjective and descriptive system that are used today in many clinical practises. To assess the intra-rater agreement, the scoring systems are used to calculate intervertebral disc degeneration or facet joint degeneration of N=20 functional spinal units on K=2 different occasions. To assess inter-rater agreement, the scoring systems are used to calculate intervertebral disc degeneration or facet joint degeneration of N=20 functional spinal units by K=4 different raters.

2.3.3 Development of a finite element model of the cervical spine

The seventh objective of this thesis is to assess the influence of prosthesis malplacement on the biomechanics of the index and adjacent levels. This model should be able to mimic normal motion, stresses and strains under physiological loading conditions. For this analysis, a three dimensional finite element model is used.
The geometry of the model is based on a MRI scan of a 29-year old male, to represent the 50^{th} age percentile of the population. From this MRI, the vertebrae are manually segmented.

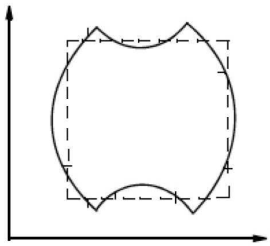

Figure 2.2: One of two breathing modes of rectangular surface element when reduced integration is used.

In this thesis, the nucleus of the intervertebral disc is modeled using nearly incompressible cubic solid elements with a poison coefficient of 0.49. However, the standard interpolation functions of the cubic elements are not capable to accurately describe the deformation field in (nearly) incompressible materials as small volumetric strains can cause a large strain energy in these elements. To cope with this phenomenon known as volume locking, reduced integration elements are chosen to model the nucleus. These elements reduce the number of integration points from eight to one. However reduced integration elements suffer from breathing modes, i.e. modes that have no effect on the strain energy of that element. This is called hourglassing. A cubic volume element has 6 breathing modes, whereas a rectangular surface element has 2 breathing modes (figure 2.2 shows one of the two breathing modes). To cope with this undesired phenomenon, hourglass control is used for all nucleus elements.
The facet joints are modeled as solid sliding contacts with Coulomb friction to simulate the low friction between the cartilage surfaces on joints. The friction coefficient μ is 0.1.
The ligaments are considered to be glued to the bony structures. The anterior longitudinal ligament and the posterior longitudinal ligament are modeled using membrane elements. They are fixed to the cranial and caudal vertebrae and slide frictionless with respect to the intervertebral discs. The flaval ligaments, the interspinous ligaments and the capsular ligaments are modeled using bar elements. One end of the ligament is fixed to the caudal vertebra, the other end to the cranial vertebra. In this thesis, all ligaments have a bilinear stress-strain relationship to mimic the stiffening of the ligaments. Moreover, all ligaments are tension-only. To enhance computational stability and reduce buckling of the ligaments, the compression stiffness is however not set to zero, but to $1/100th$ of the tension stiffness.
Generally, deformation of a material is described by the Green-Lagrange

deformation tensor Δ:

$$\Delta = \frac{1}{2}\big((Gradu)^T + Gradu + (Gradu)^T Gradu\big) \tag{2.12}$$

$$Gradu = \begin{pmatrix} \frac{\partial u_1}{\partial X_1} & \frac{\partial u_1}{\partial X_2} & \frac{\partial u_1}{\partial X_3} \\ \frac{\partial u_2}{\partial X_1} & \frac{\partial u_2}{\partial X_2} & \frac{\partial u_2}{\partial X_3} \\ \frac{\partial u_3}{\partial X_1} & \frac{\partial u_3}{\partial X_2} & \frac{\partial u_3}{\partial X_3} \end{pmatrix} \tag{2.13}$$

In this equation $Gradu$ is the material displacement gradient tensor of the relative deformation du of a material characterized by a infinitesimal vector dX. If the deformations are small, $|Gradu| << 1$, then Δ can be simplified to a linearized deformation tensor:

$$\epsilon = \frac{1}{2}\Big((Gradu)^T + Gradu\Big) \tag{2.14}$$

However, in the current model, the assumption $|Gradu| << 1$ is not valid as large deformations due occur. Therefore equation 2.12 may not be linearised and large deformations are taken into account.
The reduced integration elements with hourglass control together with the large amount of contact bodies with different contact definitions, nonlinear material properties, and large deformations have an important impact on the computational stability and complexity of the model that is developed in this thesis. Therefore some simplifications are introduced to increase usability. First to limit computation time, the vertebrae are modeled as rigid bodies. This simplification is valid as the stiffness of the vertebrae is an order of magnitude 1000 higher than the soft tissues. Modeling the vertebrae as rigid bodies decreases computation time from 21.5 hours to 8.5 hours (on a standard dualcore desktop). Moreover, the annulus of the intervertebral disc is homogenized. The annulus is a layered composite of fibers (90% collagen and 10% elastin) and a matrix of proteoglycan. Between the k different layers, the orientation ϕ of the fibers alternates between 60° and -60° with respect to the vertebral bodies. For calculation purposes, the annulus is modeled using homogenized orthotropic cubic solid elements with the following stiffness:

$$E_{h,c} = \sum_k V_{f,k} E_f sin(\phi) + V_m E_m \tag{2.15}$$

$$E_{h,r} = E_m \tag{2.16}$$

$$E_{h,a} = \sum_k V_{f,k} E_f cos(\phi) + V_m E_m \tag{2.17}$$

where E_h is the approximated orthotropic E-modulus of the annulus in the circumferential c, radial r, and axial a direction. $V_{f,k}$ and E_f are the volume fraction and E-modulus of the fibers and V_m and E_m are the volume fraction and E-modulus of the matrix, ϕ is the orientation of the fibers with respect to the vertebral bodies.
Using this model that is developed in this thesis, the influence of different suboptimal positions of the prosthesis on the biomechanical behavior of the spine will investigated in chapter 9.

Chapter 3

Assessment of lateral continuous motion patterns of the cervical spine
A technical note

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Submitted for publication in the Journal of Biomechanics (2010)

Abstract

In this technical note, a motion analysis tool for calculating lateral intervertebral continuous motion patterns in the cervical spine is presented. The quantitative motion analysis (QMA) software developed by Medical Metrics Inc. (Houston, TX, USA) has proven its value in numerous studies and served as a benchmark in the validation process. The results showed that the here proposed method was fast, repeatable (ICC>0.77) and user-undemanding. Moreover, similar accuracy compared to QMA in measuring the quantity of intervertebral motion, expressed by the range of motion (error<0.3°) and anteroposterior translation (error<0.4mm), was achieved.

3.1 Introduction

By the advent of arthroplasty technologies in the spine, the interest in accurate motion analysis tools has increased. Many studies have reported planar intervertebral motion patterns of cervical spine. Most of them used plain radiographs with the cervical spine in full flexion and full extension positions to determine these motion patterns [3, 4, 8, 10, 13, 14, 15, 24]. Reitman et al. used fluoroscopy and extracted full flexion and full extension images from the video sequence [19]. Others used fluoroscopy to measure the sagittal motion in function of the percentage of the motion cycle or in function of the number of frames [5, 7, 11, 28].
Based on full flexion and extension radiographs, the intervertebral rotational range of motion (ROM) and translation (TR) as well as the finite center of rotation can be calculated. Based on a continuous ante- or retroflexion image sequence also intervertebral continuous angular motion (CAM) and continuous translational motion (CTM) during ante- or retroflexion, as well as the instantaneous center of rotation (ICR) at each moment of time, can be calculated. These assessments provide, beside the quantity of motion, information on the quality of motion [12].
The overall error of these calculations depends on the accuracy to track identical landmarks for each vertebra in the different frames. This is a very labor-intensive, time consuming and error prone work when done manually [3, 13, 14]. Some authors have developed computerized motion analysis software [4, 15] to track the vertebrae of interest. Over the years an Food and Drug Administration (FDA) approved computer assisted tracking software (QMA) developed by Medical Metrics Inc. (Houston, TX, USA) has become the gold standard to assess invertebral motion in the cervical spine [19, 5, 2, 6, 16, 17, 18, 20, 21, 27]. This tool has a rotational error

of 0.5° (max. 1.4°) and a translation error of 0.3 mm (max. 0.8 mm) [19]. The reported interobserver errors for rotation and translation are 0.88+/-0.85° and 0.37+/-0.53 mm.
Because the QMA tool is not on-the-spot useable in daily clinical practise, our goal was to develop and validate a user-undemanding tool to assess full flexion and extension as well as continuous lateral motion patterns with noninferior accuracy.

3.2 Description

3.2.1 Geometric distortion correction

Distortions can appear in imaging applications using X-rays. Geometric distortion can be eliminated using a correction matrix. To obtain this matrix, an X-ray image of a calibration grid is taken. From this image, based on the a prior knowledge of the grid, the correction matrix can be calculated. The mapping of the original pixel coordinates (X,Y) to the corrected pixel coordinates (X',Y') is done by a fourth order polynomial transformation:

$$[X' \; Y'] = [1 \; X \; Y \; XY \; X^2 \; Y^2 \; X^2Y \; XY^2 \; X^3 \; Y^3 \; X^3Y \; X^2Y^2 \; XY^3 \; X^4 \; Y^4] \cdot T_{inv} \tag{3.1}$$

where T_{inv} is a 15-by-2 transformation matrix holding all mapping coefficients. This mapping is applied to all frames of an image sequence or to the flexion and extension radiograph prior to further analysis.

3.2.2 Tracking region of interest round each individual vertebra

Following geometric distortion correction, a template of each individual vertebra v that is to be analyzed, is obtained manually in one arbitrary frame n from the image sequence. The position of the center of the template ($x_{v,i}$,$y_{v,i}$) and the orientation of the template ($\theta_{v,i}$) in the image reference frame are tracked for each frame i of the image sequence using a rotation invariant pattern recognition algorithm. This results in a small region of interest (ROI$_{v,i}$) around each vertebra v in each frame i.

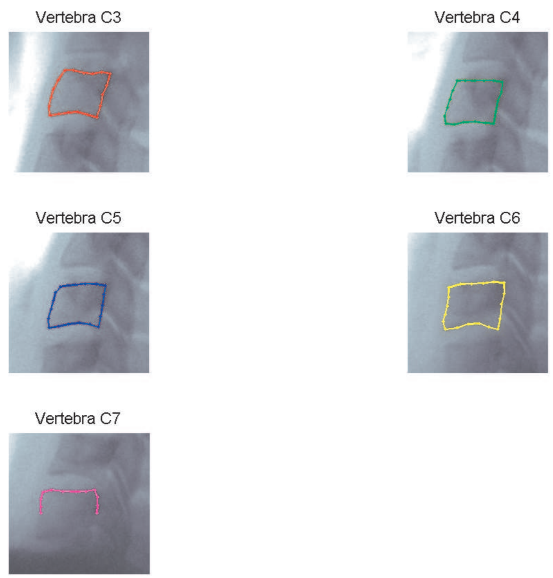

Figure 3.1: Segmented contours of each vertebra in their region of interest

3.2.3 Segmentation of the vertebrae

Using a generic model-based segmentation algorithm [22], the contours of the vertebrae v are segmented in the reference frame of their corresponding $\mathrm{ROI}_{v,i}$ (figure 3.1). For vertebra C7 only the superior part of the vertebra is segmented as the inferior part was not visible in numerous images due to the bony overlap of the shoulders on the radiographs. This step is iterated three times while increasing resolution.
This technique requires a trainingset of segmented images in order to acquire knowledge about the shape and gray-level appearance of the vertebrae. Hence thirty randomized regions of interest around each vertebra v were manually segmented to provide this training set.

3.2.4 Contour transformation

Subsequently, the contours of each vertebra v are transformed back to the original image reference frame using a planar rigid transformation:

$$\mathbf{C'}_{v,i} = R(\theta_{v,i}, \mathbf{t}_{v,i}) \cdot \mathbf{C}_{v,i}, \tag{3.2}$$

$$R(\theta_{v,i}, \mathbf{t}_{v,i}) = \begin{pmatrix} \cos(\theta_{v,i}) & \sin(\theta_{v,i}) & x_{v,i} \\ -\sin(\theta_{v,i}) & \cos(\theta_{v,i}) & y_{v,i} \\ 0 & 0 & 1 \end{pmatrix}, \tag{3.3}$$

In this equation $\mathbf{C}_{v,i}$ are the segmented contours of vertebra v in frame i in the coordinate system of $\mathrm{ROI}_{v,i}$ and $\mathbf{C}'_{v,i}$ are the transformed contours in the coordinate system of the image. $\mathrm{R}(\theta_{v,i},\mathbf{t}_{v,i})$ is the planar transformation matrix determined by a planar rotation $\theta_{v,i}$ and translation $\mathbf{t}_{v,i}$ defined by the location of $\mathrm{ROI}_{v,i}$.

3.2.5 Matching of the contours

For further analyzes, two assumptions were made. First, we assumed that there is no out-of-plane motion during flexion-extension, second, the vertebral bodies are considered to be rigid throughout the motion.
The contours of a vertebrae v in a frame i are matched with the contours of that same vertebra in an arbitrary frame q. To obtain an initialization, this matching is first realized using a least square algorithm by minimizing the following weighted equation:

$$(\mathbf{C'}_{v,q} - [R(\theta_{v,i}, \mathbf{t}_{v,i}) \cdot \mathbf{C'}_{v,i}])^T \cdot \mathbf{W} \cdot (\mathbf{C'}_{v,q} - [R(\theta_{v,i}, \mathbf{t}_{v,i}) \cdot \mathbf{C'}_{v,i}]) = 0 \tag{3.4}$$

In this equation, $\mathbf{C'}_{v,i}$ and $\mathbf{C'}_{v,q}$ are two vectors with corresponding points of the contours of a vertebra v in the arbitrary frame q and a random frame i; $R(\theta, \mathbf{t})$ is the planar transformation matrix identical to the one in equation 3.3; $\mathbf{W}$ is a diagonal matrix with weights for each corresponding point.
Because the condition of correspondence between points of the contours to be matched may not always be fulfilled, matching was improved using a iterative closest point (ICP) algorithm described by Besl and McKay [1]. This algorithm does not require corresponding points and is monotonically

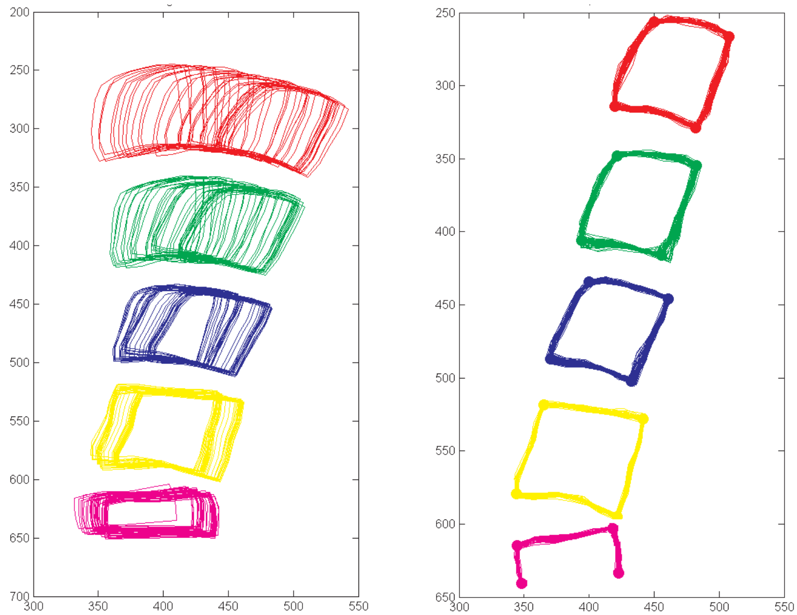

Figure 3.2: (a) Contours of the vertebrae $C'_{v,i}$, $\forall\ i$, prior to matching. (b) Contours of the vertebrae $C'_{v,i}$, $\forall\ i$, after matching to $C'_{v,q}$.

convergent, i.e. it always converges to a local minimum. To ensure convergence to the global minimum a good initialization, such as the aforementioned least square minimization, is required. The ICP algorithm fits the points of $\mathbf{C'}_{v,i}$ to the points in $\mathbf{C'}_{v,q}$ while minimizing the sum of square errors of the closest points. Figure 3.2 shows the result of such a matching procedure.
The output of the ICP algorithm provides $\alpha(v,i)$, $t_x(v,i)$, $t_y(v,i)$ which is the rotation and translation of a vertebra v in function the number of frames i with respect to the image reference frame.

3.2.6 Transformation to a physiologic reference frame

The results of the aforementioned procedure are difficult to interpret as they depend on how the cervical spine is positioned with respect to the image reference frame in the arbitrary frame n. The rotation and the anteroposterior translation of one vertebra in a coordinate system attached to the adjacent inferior located vertebra makes a clinical and biomechanical interpretation possible as described by White and Panjabi [26]. As planar rotations are invariant of the reference frame, intervertebral rotation can be calculated as follows:

$$\alpha"(v, v+1, i) = \alpha(v+1, i) - \alpha(v, i) \ \forall \ i, \tag{3.5}$$

where $\alpha(v, i)$ is the rotation of the vertebra of interest with respect to the image reference frame and $\alpha(v+1, i)$ is the rotation of the adjacent inferior located vertebra with respect to the image reference frame. The anteroposterior and craniocaudal translation ($t_x"(v, v+1, i)$ and $t_y"(v, v+1, i)$) can be defined as the translation of the center point of the vertebral body of v according to a reference frame with the x-axis coincident with the bisector between the endplates of the disc space formed by v and $v+1$ [4, 28] or to the superior endplate of the inferior vertebral body $v+1$, and can be calculated using a rigid planar transformation similar to the one described in equation 3.2.

3.2.7 Smoothing of the intervertebral motion patterns

Because intervertebral motion of the cervical spine is fluent during ante- or retroflexion, measurement noise due to segmentation, registration and calculation should be eliminated by means of a smoothing process. Therefore when calculating continuous motion patterns, a moving average filter identical to the one described by Van Mameren [11] is used in this study. Figure 3.3 shows the intervertebral and global rotation and anteroposterior translation in function of the number of frames after smoothing.

3.2.8 Outcome parameters

Finally, several quantitative parameters can be calculated. Intervertebral range of motion (ROM) is defined as the difference between maximum and minimum rotation $\alpha"$. Total anteroposterior (TR_x) and craniocaudal (TR_y) translation is defined as the difference between maximum and minimum anteroposterior and craniocaudal translation $t_x"$ and $t_y"$. The aforementioned parameters can be calculated for each intervertebral level.
By definition, rotation corresponding to flexion is positive whereas rotation corresponding to extension is negative. Also by definition, motion towards the spinal canal is considered positive translation, whereas motion away from the spinal canal is negative translation.

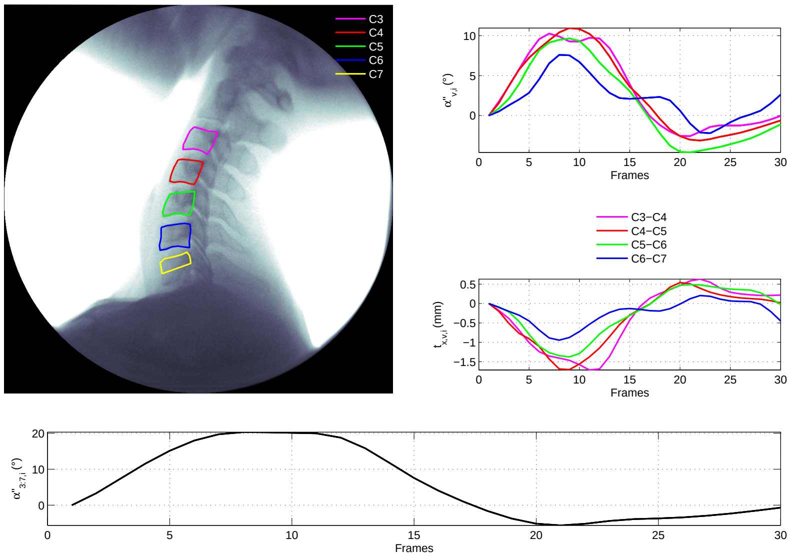

Figure 3.3: Example of intervertebral and global (C3-C6) rotation (α") and anteroposterior translation (t_x) in function of the number of frames i. Frame 0: neutral position, frame 9: full flexion position, frame 21: full extension position, frame 30: neutral position.

3.3 Validation

3.3.1 Methods

The validation of the described motion analysis tool consisted of three steps. In a first step, a study analogous to one performed by Reitman et al. [18] was done. Three cadaveric cervical spine specimen (C3-C7) were frozen in cylindrical blocks of ice with a diameter of 15 cm. The ice was used to represent the normal scatter of the soft tissues on a planar radiograph. Fluoroscopic images were taken while the specimens were manually moved in the lateral plane, 20 cm in front of the image intensifier, while out of plane motion was minimized. Every calculated intervertebral rotation α" or anteroposterior translation t_x" was considered as an error as no intervertebral motion was possible.
In a second step, the full flexion and extension motion patterns of a cohort of 30 consecutive patients operated with a Bryan Cervical Disc (Medtronic, USA)

at the university hospital Gasthuisberg (Leuven, Belgium) were calculated using QMA software and were compared with the calculated motion patterns obtained by our tool. In total, ROM and TR_x of 71 intervertebral levels were analyzed. Results were investigated using the two-sided t-test for paired measurements. The same comparison was made for the continuous motion patterns of 2 consecutive patients operated with the same device at the same hospital. ROM as well as rotation during retroflexion α" were compared between QMA and our own tool. Comparability was assessed using the coefficient of multiple determination [9].
To assess the reproducibility and reliability, ROM and TR_x of three image sequences were assessed six times by one observer, with a 2-day interval between each assessment. Intra-rater agreement, i.e. the agreement between the ratings of the same rater, was evaluated using two-way random model of intraclass correlation coefficients (ICC), with measures of absolute agreement [23]. Ninety-five % confidence intervals (CI) were constructed around each ICC [25]. The measurement error was assessed by comparison of the range of motion and anteroposterior translation of each measurement to the average ROM and TR_x of each sequence [19].

3.3.2 Results

The average calculated intervertebral rotation α" of the three frozen cervical spine specimens based on 32 frames was 0.28+/-0.75°; the average t_x" was 0.34+/-0.26 mm.
Based on the full flexion and extension radiographs, no significant difference in calculated ROM or TR_x of 71 levels of 30 patients between the QMA software and our tool were found ($p>0.82$). The mean absolute difference in ROM and TR_x was $0.95\pm1.24^\circ$ and 1.35 ± 2.72 mm (table 3.1). Based on the continuous fluoroscopic image sequences, no significant difference in calculated ROM of 6 levels of 2 patients between the QMA software and our tool was observed ($p>0.1$). The coefficient of multiple determination of α" ($p<0.05$) based on 6 intervertebral levels between the QMA software and our tool was 0.798.
Excellent intra-rater agreement was found using on the six measurements of three image sequences (ICC=0.77, CI=0.30-0.99). The average absolute error between the intervertebral rotation measured and the average intervertebral rotation for all six measurements was 0.76+/-0.43°.

Table 3.1: Absolute difference (Δ) in calculated range of motion (ROM) and anteroposterior translation (TR_x) between the QMA software (Medical Metrics Inc.) and our motion analysis tool, based on full flexion and extension radiographs.

	ROM ($^\circ$)	TR_x (mm)
n (levels)	71	71
mean(Δ)	0.95	1.35
sd(Δ)	1.24	2.72
p	0.713	0.784

3.4 Discussion

Our goal was to develop and validate a tool for the assessment of both full flexion and extension as well as continuous lateral intervertebral motion patterns that is accurate and user-undemanding. The QMA software by Medical Metrics Inc. served as a bench mark for the validation process of this tool.

The generic model-based algorithm [22] to automatically segment the contours of the vertebrae needs a training set of segmented images of the same image modality and quality and orientation of the vertebrae. Once this training set is established, the tool does not need any further manual input except for the raw identification of the vertebrae that have to be segmented in an arbitrary frame of the image sequence. The segmentation of the vertebrae combined with the calculations of the motion patterns takes up to 2 minutes for an image sequence of 60 frames on a standard laptop or desktop. This indicates that the tool is user-friendly and not time consuming.

Based on the results of the first step in validation process, the error in intervertebral rotations and translations averaged less than 0.3° and 0.4 mm and were not significant different from those obtained by Reitman et al. with the QMA software in a similar experiment ($\sim$0.35+/-0.35° and $\sim$0.25+/-0.17 mm) [18].

The results of the second validation step showed that the tool was able to calculate the ROM and TR_x based on full flexion and extension radiographs or based on fluoroscopic image sequences at least with the same accuracy as the validated QMA software. Although the coefficient of multiple determination was 0.798, there was a difference when calculation the continuous intervertebral rotation during retroflexion (α") between both measurement tools. This might be due to the smoothing algorithm which introduces a small phase shift. This phase shift does not influence the magnitude of motion and therefore ROM and TR_x remain unaffected. In addition to the aforementioned results,

excellent intra-observer agreement for the motion tool was found. Moreover, the measurement error from the repeatability study excelled those of previous studies (0.88°-1.9°) [4, 18, 28].
Besides the user-friendliness and high accuracy, the main advantage of the described tool is the ability to assess continuous intervertebral motion patterns with very limited user input. Continuous intervertebral displacements such as CAM and CTM at each moment of time can be calculated providing both information on the quantity and quality of motion. Moreover, the sagittal cadence can be investigated [12].
Apart from intervertebral motion patterns, the implemented segmentation routine also allows the calculation of geometric properties such as width and height of the vertebral bodies and intervertebral disc height. Moreover, the tool can be augmented to assess the amount of subsidence or migration of spine arthroplasty devices.
A drawback of this method is that it requires a training set of segmented images. The quality and accuracy of the manual delineations of the vertebral bodies will influence the segmentation results and, although excellent intra-rater agreement was achieved, it should be carefully executed. However, once the training set is in place, the segmentation is user independent.

3.5 Conclusion

In this study, a tool was developed and validated that can be used for the assessment of lateral full flexion and extension as well as continuous intervertebral motion. Because the tool is user-undemanding and as accurate as the current gold standard in motion analyzes, it might be used in clinical practise and scientific research.

Acknowledgments

Medtronic (Memphis, TN, USA) is acknowledged for the institutional research and education grant. Medical Metrics Inc. (Houston, TX, USA) is gratefully acknowledged for providing the data and collaboration needed for the validation process.
The fluoroscopy work of Jan Leemans and Guido Pauwels of the Division of Radiology (University hospital Gasthuisberg, Leuven, Belgium) is very much appreciated.

Author's involvement

All authors, Joris Walraevens, Dieter Seghers, PhD, Philippe Demaerel, MD, PhD, Paul Suetens, PhD, Jan Goffin, MD, PhD, and Jos Vander Sloten, PhD, were substantially involved in this multidisciplinary research. The tool was developed by Joris Walraevens and Dieter Seghers. The development was coordinated by Paul Suetens and Jos Vander Sloten. The validation and data analysis was performed by Joris Walraevens and was supervised by Jos Vander Sloten and Jan Goffin. Radiological imaging of the volunteers was coordinated by Philippe Demaerel. This manuscript was written up by Joris Walraevens and was reviewed by all authors.

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Chapter 4

Qualitative and quantitative assessment of degeneration of cervical intervertebral discs and facet joints

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Adapted from a manuscript published inthe European Spine Journal 18(3), 358-370 (2009)

Abstract

Introduction Degeneration of intervertebral discs and facet joints is one of the most frequently encountered spinal disorders. In order to describe and quantify degeneration and to evaluate a possible relationship between degeneration and biomechanical parameters, e.g. the intervertebral range of motion and intradiscal pressure, a scoring system for degeneration is mandatory. However, few scoring systems for the assessment of degeneration of the cervical spine exist. Therefore two separate objective scoring systems to qualitatively and quantitatively assess the degree of cervical intervertebral disc and facet joint degeneration were developed and validated.

Methods The scoring system for cervical disc degeneration consists of three variables which are individually scored on neutral lateral radiographs: 'Height loss' (0-4 points), 'Anterior osteophytes' (0-3 points) and 'Endplate sclerosis' (0-2 points). The scoring system for facet joint degeneration consists of four variables which are individually scored on neutral computed tomography scans: 'Hypertrophy' (0-2 points), 'Osteophytes' (0-1 point), 'Irregularity' on the articular surface (0-1 point) and 'Joint space narrowing' (0-1 point). Each variable contributes with varying importance to the overall degeneration score (max. 9 points for the scoring system of cervical disc degeneration and max. 5 points for facet joint degeneration). Degeneration of 20 discs and facet joints of 20 patients was blindly assessed by 4 raters: 2 neurosurgeons (1 senior and 1 junior) and 2 radiologists (1 senior and 1 junior), firstly based on first subjective impression and secondly using the scoring systems. Measurement errors and inter- and intra-rater agreement were determined.

Results The measurement error of the scoring system for cervical disc degeneration was 11.1% versus 17.9% of the subjective impression results. This scoring system showed excellent intra-rater agreement (ICC=0.86, 0.75-0.93) and excellent inter-rater agreement (ICC=0.78, 0.64-0.88). Surgeons as well as radiologists and seniors as well as juniors obtained excellent inter- and intra-rater agreement. The measurement error of the scoring system for cervical facet joint degeneration was 20.1% versus 24.2% of the subjective impression results. This scoring system showed good intra-rater agreement (ICC=0.71, 0.42-0.89) and fair inter-rater agreement (ICC=0.49, 0.26-0.74). Both scoring systems fulfilled the criteria for recommendation proposed by Kettler and Wilke.

Conclusions Our scoring systems can reliable and objective tools for assessing cervical disc and facet joint degeneration. Moreover, the scoring system of cervical disc degeneration showed to be experience- and discipline-independent.

4.1 Background

Degeneration of intervertebral discs and facet joints is one of the most frequently encountered spinal disorders [17]. In order to describe and quantify degeneration and to evaluate a possible relationship between degeneration and biomechanical parameters, e.g. the intervertebral range of motion, sagittal alignment and intradiscal pressure, a scoring system is mandatory. Moreover, a scoring system can be a helpful tool to investigate the possible correlation between intervertebral disc degeneration and facet joint degeneration or to assess the evolution of degeneration over time after an arthrodesis or after arthroplasty. However, up to date a limited amount of scoring systems for degeneration of cervical intervertebral discs and facet joints based on radiographs have been developed [9]. Two scoring systems for cervical disc degeneration have been tested for reliability (Kellgren et al. [8] by Côté et al. [3] and Kettler et al. [10]). Only one scoring system for facet joint degeneration has been tested for reliability (Kellgren et al. [8]). In their review Kettler and Wilke observed a wide variety in design and terminology of the existing scoring systems [9]. One of the major drawbacks of the scoring systems of Kellgren for cervical disc and facet joint degeneration is the use of subjective, descriptive terms as 'moderate' and 'severe' to quantify degeneration. To ensure objectivity, Kettler et al. developed a numerical radiographic scoring system for cervical intervertebral disc degeneration [10]. In this scoring system three variables: 'height loss' of intervertebral disc height, 'osteophyte formation' and 'diffuse sclerosis' have to be graded individually on a scale from 0 to 3. Based on the sum, the overall degree of disc degeneration is determined. Although Kettler and Wilke obtained substantial inter-rater agreement ($\kappa = 0.688$), the scoring system has some drawbacks. Firstly, the scoring system is difficultly applicable in daily clinical practice because it is complex and time-consuming. Secondly, the scoring system was developed based on the lateral radiographs of human cadaveric osseoligamentous spine specimens. It has not been tested in vivo. A reliable scoring system for the assessment of cervical facet joint degeneration does not exist up to date. Kellgren et al. used lateral radiographs to score the degeneration of cervical facet joints [8]. Côté et al. found an unacceptable inter-rater agreement for this scoring system (ICC=0.45) [3]. They claimed that one of the reasons for this poor agreement was that lateral radiographs often poorly visualize the facet joints. Computed tomography scans might improve the visibility and therefore early degenerative change might be better detected. The goal of this study is to establish and validate a quantitative scoring system for cervical intervertebral disc degeneration based on lateral radiographs and a scoring system for cervical facet joint degeneration based on computed tomography scans. The results of these scoring systems are compared with results based on first subjective impression. Moreover, as an application of both scoring systems, the spatial correlation between facet joint degeneration and intervertebral disc degeneration is investigated.

4.2 Materials and methods

4.2.1 Scoring system for cervical disc degeneration based on lateral radiographs

The scoring system for cervical disc degeneration consists of three variables with decreasing importance to the total degeneration score: 'Height loss', 'Anterior osteophytes', and 'Endplate sclerosis'. Each of these variables is individually scored. Next, the three variables are summed to obtain the overall degree of disc degeneration (ranging from 0 to 9; table 4.1). Height loss is defined as the middle disc height with respect to a normal middle disc height at an adjacent level. Height loss is graded from 0 to 4. Middle disc height of the target level is assessed with respect to the middle disc height of a normal adjacent level (figure 4.1). The length of the anterior osteophytes is measured with respect to the anteroposterior diameter of the corresponding vertebral body, which is measured at the middle of the vertebral body (figure 4.2). Anterior osteophytes are scored from 0 to 3. When different scores are attributed to the cranial and caudal anterior corners of the target level, the highest score is chosen. For endplate sclerosis, a distinction between no apparent sclerosis, just detectable and definite sclerosis is made (score 0 to 2, figure 4.3).

4.2.2 Scoring system for cervical facet joint degeneration based on computed tomography scans

The scoring system for degeneration of the facet joints consists of four variables with varying importance to the total score: 'Hypertrophy', 'Osteophytes', 'Irregularity' of the articular surface, and 'Joint space narrowing'. These variables are assessed on computed tomography scans. Similarly to the scoring system for cervical disc degeneration, each of these variables is individually scored. Next, the four variables are summed to obtain the overall degree of facet joint degeneration (ranging from 0 to 5; see table 4.2).
Hypertrophy is graded from 0 to 2. Zero points are given when there is no hypertrophy present; 1 point when hypertrophy is visible on one of the margins of the articular surface; and 2 points when it is present on all margins (figure 4.4). Osteophytes are graded 0 if no osteophytes are present and 1 if osteophytes are present (figure 4.5). Irregularity of the articular surface is

Table 4.1: Scoring system of cervical disc degeneration based on neutral lateral radiographs. VB: vertebral body; AP: anteroposterior.

1. Height loss†	0%	0 points
Middle disc height compared	≤25%	1 points
to normal middle disc height	>25% - ≤50%	2 points
at an adjacent level	>50% - ≤75%	3 points
	>75%	4 points
2. Anterior osteophytes	No osteophytes	0 points
with respect to the AP diameter	≤ 1/8 AP diameter	1 point
of the corresponding VB	> 1/8 - ≤ 1/4 AP diameter	2 points
	> 1/4 AP diameter	3 points
3. Endplate sclerosis	No sclerosis	0 points
	Detectable	1 point
	Definite	2 points
Overall degree of disc degeneration	0 points (no degeneration)	
= 1 + 2 + 3	1-3 points (mild degeneration)	
	4-6 points (moderate degeneration)	
	7-9 points (severe degeneration)	

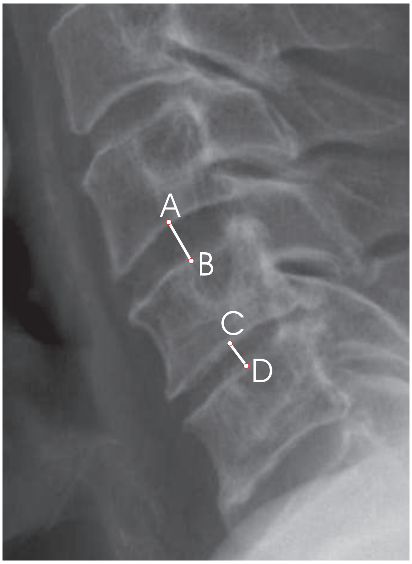

Figure 4.1: Height loss is assessed on lateral radiographs. Middle disc height of the target level (CD) is compared to the middle disc height of a normal adjacent level (AB). No height loss is scored as 0; a loss in disc height less than 25% receives 1 point; height loss between 25% and 50% receives 2 points; between 50% and 75% 3 points; and 4 points are given when the height loss is more than 75%.

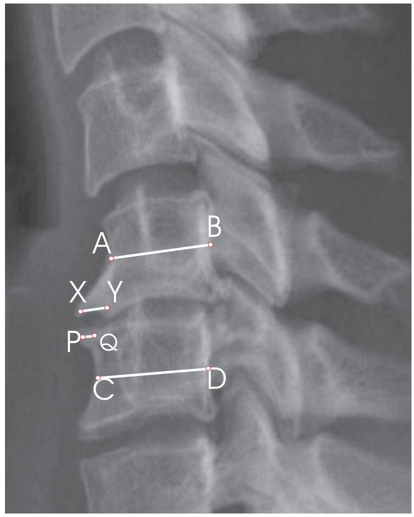

Figure 4.2: Anterior osteophytes are assessed on lateral radiographs. The length of the anterior osteophytes (XY and PQ) is measured with respect to the anteroposterior diameter of the vertebral body (AB and CD respectively). When no anterior osteophyte is visible, a score of 0 is attributed; an anterior osteophyte that is just detectable receives 1 point; an anterior osteophyte which extends less than one forth of the anteroposterior diameter receives 2 points; when the anterior osteophytes extends more than one forth, 3 points are attributed. The highest of the cranial and caudal score is used as final score.

A B C

Figure 4.3: Endplate sclerosis is assessed on lateral radiographs. Zero points are attributed as no endplate sclerosis is present (A); 1 point is given if sclerosis is just detectable (B); 2 points are given when sclerosis is definitively present at the cranial and/or the caudal endplate.

Table 4.2: Scoring system of cervical facet joint degeneration based on computed tomographs scans FJ: facet joint

1. Hypertrophy of FJ	None	0 points
	On one of the margins of the articular surfaces	1 point
	On all margins of the articular surfaces	2 points
2. Osteophytes on FJ	None	0 points
	Yes	1 point
3. Irregularity on articular surface	Normal	0 points
	Irregular	1 point
4. Joint space narrowing	Normal	0 points
	Narrowed	1 point
Overall degree of facet joint degeneration = 1 + 2 + 3 + 4	0 points (no degeneration)	
	1 point (mild degeneration)	
	2-3 points (moderate degeneration)	
	4-5 points (severe degeneration)	

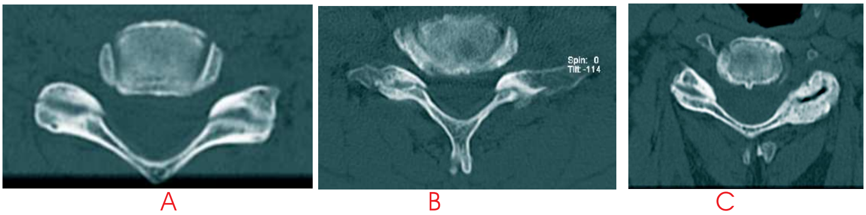

Figure 4.4: Hypertrophy is assessed on transverse computed tomography scans. Zero points are given when no hypertrophy is present (A); 1 point when hypertrophy is present on one of the margins of the articular surface (B); and 2 points when it is present on all margins (C).

scored 0 if the articular surface is smooth; and is scored 1 if the articular surface is irregular (figure 4.6). If the joint space of both facet joints is not narrowed, joint space narrowing is scored 0. In case of narrowing, it is scored 1 (figure 4.7). If a difference in degeneration score between the left and right facet joint is found, the highest of both scores is used.

4.2.3 Experimental procedure

In a retrospective study, neutral lateral radiographs and computed tomography scans of twenty patients, recently operated for cervical degenerative disc

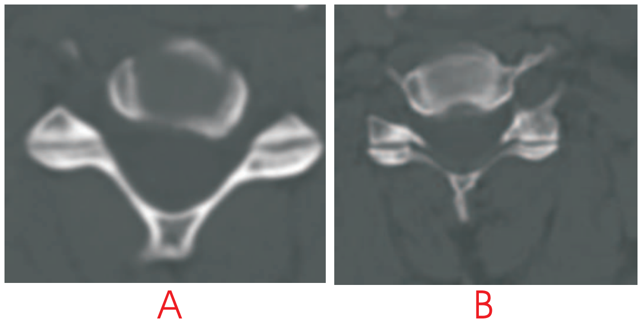

Figure 4.5: Osteophytes are assessed on transverse computed tomography scans. Zero points are given when no osteophytes on either of the facet joints are visible (A); 1 point when osteophytes are present (B).

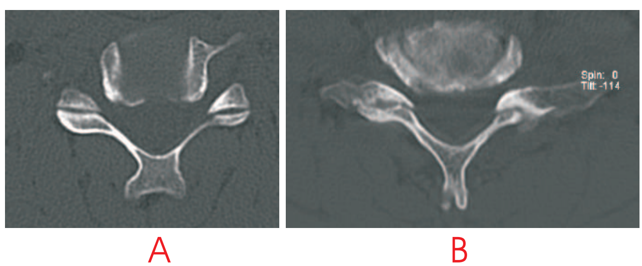

Figure 4.6: Irregularity of the articular surface is assessed on transverse computed tomography scans. Zero points are given when the articular surface of either of the facet joints is smooth (A); 1 point when the surface is irregular (B).

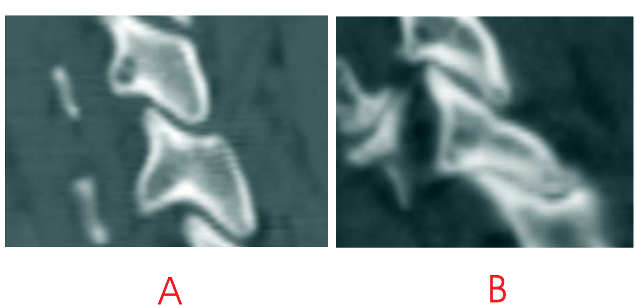

Figure 4.7: Joint space narrowing is assessed on computed tomography scans. Zero points are given when the joint space of either of the facet joints is not narrowed (A); 1 point when the space is narrowed (B).

Table 4.3: Overall degree of degeneration of cervical disc and facet joints based on first subjective impression

Indication
No degeneration
Mild degeneration
Moderate degeneration
Severe degeneration

disease, were used for the assessment of intervertebral disc and facet joint degeneration. The name of each patient was removed and the clinical history remained unknown to prevent bias.
Twenty intervertebral discs and facet joints of the operated level were analyzed by four raters: two neurosurgeons (one senior and one junior) and two radiologists (one senior and one junior). None of the raters were previously connected to the study. Written instructions were provided to all raters before the assessment. No assistance was given during the assessment.
Intervertebral disc degeneration and facet joint degeneration were assessed three times: firstly based on subjective impression (SI; see table 4.3), followed by a second time using the scoring systems (SS 1). After one month, the raters were asked to reassess all levels a third time using the scoring systems (SS 2). Between all assessments, the order was randomized to prevent bias.
Intervertebral disc degeneration was scored based on neutral lateral radiographs; facet joint degeneration for the operated level was assessed on computed tomography scans.

4.2.4 Statistical analysis

The measurement error was estimated using within-subject standard deviations based on the SI and SS 1 results. The measurement error is a measure for the variation in the scoring system [1,2]. Ninety-five % prediction limits can be calculated using the measurement error. The difference between the observed value and the measured value is expected to be less than this value in 95% of the observations.
Inter-rater agreement, i.e. the agreement between the ratings of all raters, and the intra-rater agreement, i.e. the agreement between the ratings of the same rater, were evaluated using two-way random model of intraclass correlation coefficients (ICC), with measures of absolute agreement [18]. A single measure intraclass correlation was selected to estimate the reliability of a single rating instead of a mean of several ratings. Inter-rater agreement was assessed based

Table 4.4: Convention for inter- and intra-rater agreement according to Fleiss et al [5]. ICC: Intra-class correlation coefficient

ICC	Strength of agreement
ICC $\leq$ 0.40	poor agreement
0.40 $<$ ICC $\leq$ 0.60	fair agreement
0.60 $<$ ICC $\leq$ 0.75	good agreement
0.75 $<$ ICC	excellent agreement

Table 4.5: Measurement error of cervical disc degeneration based on the assessment of 20 intervertebral discs (relative within subject standard deviation (WSSD) and 95% prediction limit (PL))

	Scale	WSSD	95% PL
Subjective impression of the overall degree of disc degeneration		0.179	1.051
Height loss	0-4	0.123	0.964
Anterior osteophytes	0-3	0.172	1.012
Endplate sclerosis	0-2	0.339	1.327
Overall degree of disc degeneration	0-9	0.111	1.960

on the SI and SS 1 results. Intra-rater agreement was calculated based on the SS 1 and SS 2 results. Ninety-five % confidence intervals (CI) were constructed around each ICC [19]. Table 4.4 provides the convention that is used throughout the text.
Linear correlations were investigated using Pearson r correlation coefficients. Data analysis was performed using Statistica 6.0.

4.3 Results

4.3.1 Disc degeneration

Measurement error

The scoring system shows an improved measurement error for the overall degree of disc degeneration the with regard to the SI result (11.1% versus 17.9%; table 4.5). The variable 'endplate sclerosis' has the largest measurement error (33.9%).

Table 4.6: Inter-rater agreement between all raters based on the assessment of 20 intervertebral discs (Intra-class correlation coefficients (ICC) and 95% confidence intervals (CI))

	ICC	95% CI	
Subjective impression of the overall degree of disc degeneration	0.7650	0.5913	0.8874
Height loss	0.7284	0.5403	0.8673
Anterior osteophytes	0.7275	0.5813	0.8586
Endplate sclerosis	0.3107	0.1273	0.5582
Overall degree of disc degeneration	0.7759	0.6421	0.8871

Table 4.7: Intra-rater agreement between two assessments (SS 1 and SS 2) of all raters based on the assessment of 20 intervertebral discs (Intra-class correlation coefficients (ICC) and 95% confidence intervals (CI))

	ICC	95% CI	
Height loss	0.8039	0.6036	0.9137
Anterior osteophytes	0.7869	0.5847	0.9034
Endplate sclerosis	0.6156	0.3978	0.8010
Overall degree of disc degeneration	0.8580	0.7461	0.9338

Inter-rater agreement

The inter-rater agreement for the overall degree of disc degeneration of the scoring system is excellent (ICC=0.78, 0.64 - 0.88; table 4.6). The ICC of the variable 'endplate sclerosis' is poor (ICC= 0.31 versus 0.73 for height loss and anterior osteophytes). The overall degree of disc degeneration shows a small improvement in ICC with respect to the SI results (ICC=0.77, 0.59 - 0.89).

Intra-rater agreement

Excellent intra-rater agreement is observed for the overall degree of disc degeneration (ICC= 0.86, 0.75 - 0.93; table 4.7). This observations holds for all variables individually, except for endplate sclerosis which has a good intra-rater reliability (ICC= 0.62, 0.40 - 0.80).

Comparison between raters with different experience

A comparison between experienced and unexperienced raters was made. Senior raters obtained better inter-rater agreement than junior raters for the variables

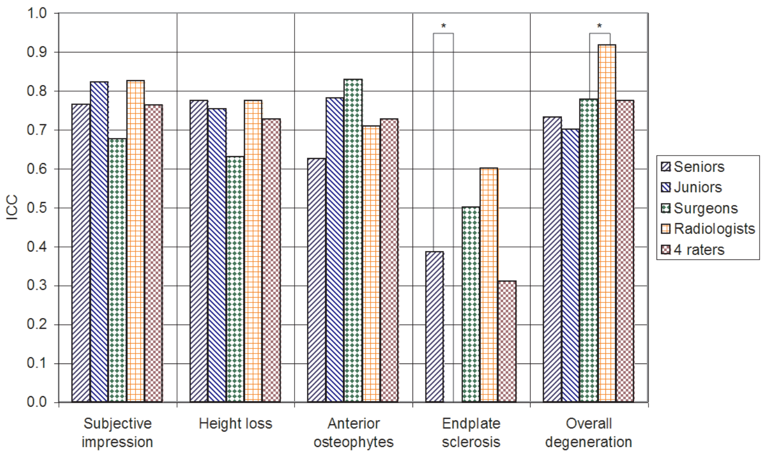

Figure 4.8: Inter-rater agreement between senior versus junior raters and surgeons versus radiologists and between all raters based on the assessment of 20 intervertebral discs (Intra-class correlation coefficients (ICC);$^{*}p<0.05$).

height loss and endplate sclerosis (figure 4.8). Junior raters showed better inter-rater agreement for the SI results and anterior osteophytes. For all variables, except for endplate sclerosis, junior as well as senior raters obtained excellent intra-rater agreement (figure 9), with best results for the junior raters.
Junior as well as senior raters obtained good inter-rater and excellent intra-rater agreement for the overall degree of disc degeneration ($p>0.05$).

Comparison between raters of different disciplines

A comparison between raters of different disciplines was made: one senior and one junior surgeon versus one senior and one junior radiologist. The radiologists obtained better inter-rater agreement for the overall degree of disc degeneration ($p<0.05$). The inter-rater agreement of all variables was better for the radiologists, except for anterior osteophytes. The intra-rater agreement of all variables was better for the radiologists, except for height loss.
Surgeons as well as radiologists obtained excellent inter-rater and intra-rater agreement for the overall degree of disc degeneration (figures 4.8 and 4.9).

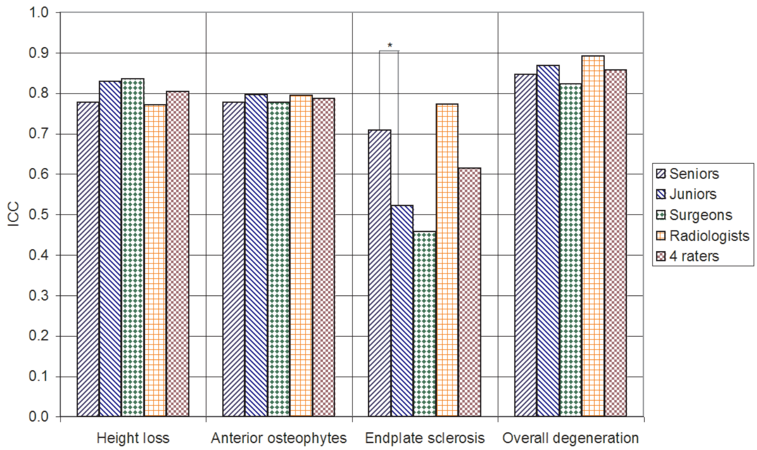

Figure 4.9: Intra-rater agreement between two assessments (SS 1 and SS 2) of senior versus junior raters and surgeons versus radiologists and of all raters based on the assessment of 20 intervertebral discs (Intra-class correlation coefficients (ICC); $^*p<0.05$)

Table 4.8: Measurement error of cervical facet joint degeneration based on the assessment of 20 facet joints (relative within subject standard deviation (WSSD) and 95% Prediction limit (PL)

	Scale	WSSD	95% PL
Subjective impression of the overall degree of facet joint degeneration		0.243	1.426
Hypertrophy	0-2	0.304	1.191
Osteophytes	0-1	0.401	0.786
Irregularities	0-1	0.436	0.855
Joint space narrowing	0-1	0.393	0.771
Overall degree of facet joint degeneration	0-5	0.201	1.966

4.3.2 Facet joint degeneration

Measurement error

The overall degree of facet joint degeneration shows an improved measurement error in comparison to the SI result (20.1% versus 24.2%; table 4.8). Nevertheless, the measurement errors remain large for the overall degree of facet joint degeneration (20.1%) and all of the variables individually (39.3%-43.6%).

Table 4.9: Inter-rater agreement between all raters based on the assessment of 20 facet joints (Intra-class correlation coefficients (ICC) and 95% confidence intervals (CI))

	ICC	95% CI	
Subjective impression of the overall degree of facet joint degeneration	0.3494	0.1647	0.5902
Hypertrophy	0.1708	0.0000	0.4759
Osteophytes	0.3979	0.1707	0.6817
Irregularities	0.2031	0.0128	0.5139
Joint space narrowing	0.4007	0.1769	0.6837
Overall degree of facet joint degeneration	0.4866	0.2589	0.7449

Table 4.10: Intra-rater agreement between two assessments (SS 1 and SS 2) of all raters based on the assessments of 20 facet joints (Intra-class correlation coefficients with 95% confidence intervals (CI))

	ICC	95% CI	
Hypertrophy	0.5596	0.2400	0.8161
Osteophytes	0.6568	0.3818	0.8576
Irregularities	0.5443	0.2106	0.8040
Joint space narrowing	0.5176	0.2067	0.7902
Overall degree of facet joint degeneration	0.7167	0.4230	0.8894

Inter-rater agreement

Poor inter-rater agreement for the SI results (ICC=0.35, 0.16 - 0.59; table 4.9) and fair inter-rater agreement of the overall degree of facet joint degeneration (ICC=0.49, 0.26 - 0.74) is obtained. Joint space narrowing was the variable with the highest inter-rater agreement (ICC=0.40 compared to 0.17, 0.39 and 0.20 for hypertrophy, osteophytes and irregularity).

Intra-rater agreement

Good intra-rater agreement was obtained for the overall degree of facet joint degeneration (ICC=0.72, 0.42 - 0.89). However, for the variables individually, with exception of osteophytes, fair intra-rater agreement was found (table 4.10).

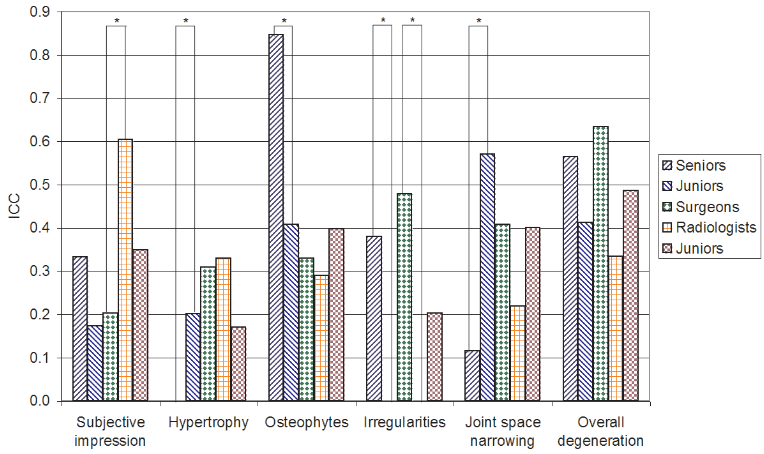

Figure 4.10: Inter-rater agreement between senior versus junior raters and surgeons versus radiologists and between all raters based on the assessment of 20 facet joints (Intra-class correlation coefficients (ICC); $^*p<0.05$)

Comparison between raters with different experience

A comparison between experienced and unexperienced raters was made. Senior raters obtained better inter-rater agreement than junior raters for the SI results and the overall degree of facet joint degeneration (figure 4.10).
Senior raters obtained excellent intra-rater agreement for the overall degree of facet joint degeneration, juniors obtained good agreement ($p<0.05$; figure 4.11).

Comparison between raters of different disciplines

A comparison between raters of different disciplines was made: one senior and one junior surgeon versus one senior and one junior radiologist. Surgeons obtained better inter-rater agreement than radiologists for the overall degree of facet joint degeneration and all of its variables, except hypertrophy (figure 4.10). The surgeons obtained good inter-rater and excellent intra-rater agreement for the overall degree of facet joint degeneration; the radiologist fair and good agreement respectively (figure 4.11).

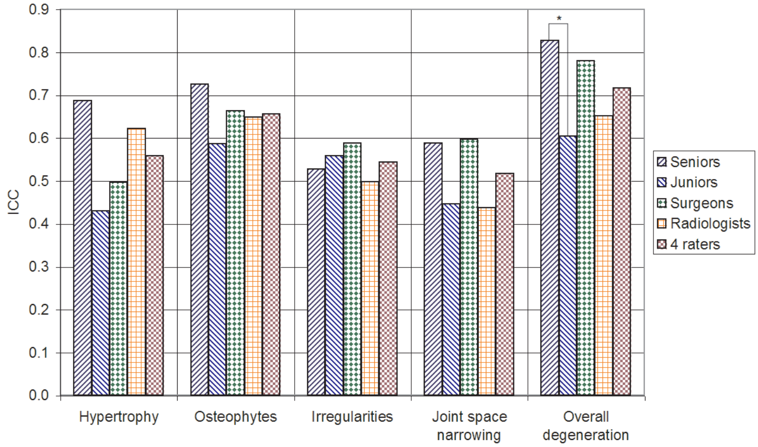

Figure 4.11: Intra-rater agreement between two assessments (SS 1 and SS 2) of senior versus junior raters and surgeons versus radiologists and of all raters based on the assessment of 20 facet joints (Intra-class correlation coefficients (ICC); $^*p<0.05$)

4.3.3 Correlation between cervical disc and facet joint degeneration

As shown in table 4.11, a significant but weak correlation is observed between disc and facet joint degeneration based on the SI results (Pearson r: 0.33, $p<0.05$) as well as based on total degeneration scores of disc and facet joint degeneration (Pearson r: 0.27, $p<0.05$).

4.4 Discussion

In this study separate scoring systems for cervical intervertebral disc and facet joint degeneration were proposed and tested for inter- and intra-rater agreement. Using these scoring systems, the spatial correlation between disc and facet joint degeneration was assessed.

In this study separate scoring systems for cervical intervertebral disc and facet joint degeneration were proposed and tested for inter- and intra-rater agreement. Using these scoring systems, the spatial correlation between disc and facet joint degeneration was assessed.

Our scoring system for cervical intervertebral disc degeneration has some similarities with the scoring system of Kettler et al. [10]. Three variables have to be graded individually on a numerical scale based on objective criteria; the sum of these scores assigns the overall degree of degeneration. Nevertheless, our scoring system is fundamentally different. In contrast to the scoring system of Kettler et al., only middle disc height is used to calculate height loss, because the anterior and posterior height are often influenced by osteophytes. Moreover, only anterior osteophytes, but no posterior osteophytes, are assessed in our scoring system, because posterior osteophytes are identified with great difficulty in lateral radiographs, due to bony overlaps. A third difference is that the variables contribute to the overall degree of degeneration with variable importance. Height loss of the middle disc height has the highest importance (four points on a nine point scale), followed by anterior osteophytes and endplate sclerosis (three and two points on a nine point scale). This strategy was chosen because height loss is a straightforward and accurate indicator for disc degeneration. In contrast to posterior osteophytes, which are often not clearly visible on lateral radiographs due to the overlap with the lateral processes, anterior osteophytes are easily scored. Anterior osteophytes have however less clinical importance and therefore lower importance than for height loss was assigned in our scoring system. Endplate sclerosis contributes to disc degeneration, but the scoring of endplate sclerosis is very sensitive to the quality of the radiographs and the proper alignment of the intervertebral disc. Therefore the lowest importance was attributed to endplate sclerosis.
These modifications did not lead to a lower inter-rater agreement. On the contrary, a stronger inter-rater agreement was observed. According to Kettler and Wilke, the inter-rater reliability of the scoring system fulfills their criterion for recommendation (ICC>0.60: at least substantial agreement according to Landis et al. [13]) [9].

Table 4.11: Correlation table of Pearson r coefficients of intervertebral disc degeneration versus facet joint degeneration based on the subjective impression (SI) results and the scoring systems. Significant correlations ($p<0.05$) are displayed in **bold**.

	SI disc	Height loss	Anterior osteophytes	Endplate sclerosis	Overall disc
SI facet joint	**0.33**	0.22	0.04	0.10	0.19
Hypertrophy	**0.36**	0.26	0.08	0.20	**0.27**
Osteophytes	0.45	**0.38**	0.10	0.21	**0.35**
Irregularities	0.14	0.23	-0.09	-0.11	0.03
Joint space narrowing	-0.01	0.02	-0.07	0.07	0.01
Overall (facet)	**0.38**	0.36	0.02	0.16	**0.27**

In addition to the inter-rater agreement, also intra-rater agreement of the scoring system for intervertebral disc degeneration was calculated. This value is a measure for the reproducibility of the scoring system. Excellent intra-rater agreement was observed for our scoring system.

A drawback of this study is that no validation of the scoring system against a gold standard was performed. The excellent inter- and intra-rater agreement indicates that the scoring system is highly reliable and repeatable. However, such agreement does not eliminate the possibility of a systematic error (consistent over- or underestimation of the 'real' degree of degeneration). Kettler and Wilke validated their scoring system based on lateral radiographs of human cadaveric osseoligamentous spine specimens, and used macroscopic slices of the respective cadaveric specimens to assess the 'real' degree of degeneration. They found that the 'real' degree of disc degeneration was underestimated in 64% of all discs [10]. However, the use of cadaveric specimen might have influenced the results. The surrounding soft tissues that can decrease visibility of the intervertebral disc space are removed. And in contrast to in vivo measurements, a long exposure time can be used. This increases contrast on the lateral radiographs, providing a better visibility.

Next to cadaveric specimens, MRI might have been used as a comparative method to further validate our scoring system. Several scoring systems have been developed to assess cervical intervertebral disc degeneration based on MRI [2, 11, 15]. Miyazaki et al. claimed that MRI is the most sensitive method for the clinical assessment of intervertebral disc pathology [15]. They reported excellent intra-rater reliability and good to excellent inter-rater reliability for their scoring system. Similar to this study, Miyazaki et al. limited the validation of their scoring system to inter- and intra-rater reliability testing. No comparison against a gold standard, such as cadaveric specimens, was made. Four spinal surgeons acted as observers in their study; no information on their experience was given. In our study, both surgeons and radiologists, juniors as well as seniors acted as observers, illustrating the multi-experience and multi-discipline use of our scoring system. Christe et al. reported that both radiographs and MRI are significantly, but weakly, correlated with histology ($r=0.33$ and $r=0.49$, $p<0.05$) in the detection of pathologic lesions in the cervical spine [2]. They did however not report on the correlation between MRI and planar radiographs. As this is a retrospective study, no MRI was available for all patients. A comparison of our scoring system with MRI could therefore not be made.

As this scoring system uses standard lateral radiographs, and as it requires uncomplicated input for the user, the scoring system can easily be used in daily clinical practice for the assessment of cervical disc degeneration. Senior and junior raters obtained good inter-rater agreement and excellent intra-rater agreement. Surgeons and radiologists obtained excellent inter- and intra-rater

agreement. These results indicate that the scoring system can be reliably used by both experienced as inexperienced raters from different disciplines.
Only one scoring system for facet joint degeneration has previously been tested for reliability (Kellgren et al. [8] by Côté et al. [3]). Fair inter-rater agreement was found (ICC=0.45). In contrast to Côté et al., who believed that this level of agreement is not acceptable for rigorous outcomes research [3], Kettler and Wilke noted that it fulfilled their criteria for recommendation (ICC>0.40: at least moderate agreement according to Landis et al. [13]) [9]. According to this criterion, also our scoring system for the assessment of facet joint degeneration (ICC=0.49), can be recommended.
Our scoring system assesses the presence of hypertrophy, osteophytes, irregularities on the articular surface and joint space narrowing at the target level based on computed tomography scans.
Similar to the scoring system of cervical disc degeneration, a drawback of this study is that the scoring system for cervical facet joint degeneration is not compared with a gold standard, such as cadaveric specimens, or is not compared to an alternative method, such as MRI.
As a clinical application, this scoring system is very useful when degeneration of one patient has to be assessed and compared at different time intervals, e.g. to investigate the influence of an arthrodesis or arthroplasty on the degeneration of the levels adjacent to the treated level. Moreover, this scoring system is applicable when degeneration of different patients on a certain timepoint has to be compared. In these cases of relative comparison, a possible systematic error is canceled out.
As an additional application for both scoring systems, the spatial correlation between intervertebral disc and facet joint degeneration has been investigated. In contrast to the lumbar spine [4, 1, 6, 7, 14, 12, 16, 18, 20], this correlation has not been thoroughly investigated for the cervical spine. A weak but significant spatial correlation between cervical intervertebral disc degeneration and facet joint degeneration was observed. However, as this was not a follow-up study, the temporal correlation could not be identified. Therefore the hypothesis that 'disc degeneration precedes facet joint osteoarthritis' [1, 6, 20] can not be confirmed, nor denied.

4.5 Conclusion

Our scoring system for cervical disc degeneration can be a reliable and objective tool. Moreover, this scoring system showed to be experience- and discipline-independent. Our scoring system for facet joint degeneration, which is based on computed tomography scans, is less reliable. Nevertheless, it fulfils the criteria for recommendation proposed by Kettler and Wilke.

A weak spatial correlation between cervical intervertebral disc and facet joint degeneration has been observed.

Acknowledgments

Medtronic (Memphis, USA) is acknowledged for the institutional research and education grant.

Author's involvement

All authors, Joris Walraevens, Baoge Liu, MD, Joke Meersschaert, MD, Philippe Demaerel, MD, PhD, Hans Delye, MD, PhD, Bart Depreitere, MD, PhD, Jos Vander Sloten, and Jan Goffin, MD, PhD were substantially involved in this multidisciplinary research. The scoring systems were developed by Joris Walraevens and Baoge Liu. The radiological images were collected by Baoge Liu. Imaging of the patients was coordinated by Philippe Demaerel and Jan Goffin. The validation of the scoring systems was done by Joke Meerschaert, Philippe Demaerel, Hans Delye and Bart Depreitere. The validation and data analysis was performed by Joris Walraevens and was supervised by Jos Vander Sloten and Jan Goffin. This manuscript was written up by Joris Walraevens and was reviewed by all authors.

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Chapter 5

Motion patterns of the cervical spine and their correlation with intervertebral disc degeneration

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To be submitted for publication in Spine

Abstract

Objective The scope of this study is to investigate quantitative and qualitative motion patterns of the cervical spine during flexion/extension, lateral bending and axial rotation of asymptomatic volunteers of different ages and to look at possible correlations between disc degeneration and intervertebral motion.

Methods Sixty asymptomatic volunteers were equally divided into four age-groups (group I: 18-30 years; group II: 31-40 years; group III: 41-50 years; group IV: 51-60 years). Based on lateral and anteroposterior fluoroscopic image sequences, global (C3-C6) and intervertebral continuous angular motion (CAM), continuous translational motion (CTM) as well as global and intervertebral range of motion (ROM), translation and the center of rotation (COR) were measured with high accuracy during flexion/extension, lateral bending and axial rotation. Intervertebral disc degeneration was scored using an objective and validated scoring system. This scoring system consists of three variables which are individually scored on lateral radiographs: height loss, anterior osteophytes and endplate sclerosis. Each variable contributes to the total degeneration score (max. 9 points).

Results There was no significant difference in intervertebral ROM nor in CAM between the age groups for any of the movements ($p<0.05$). Global ROM during flexion/extension differed significantly between group I and IV ($48.64+/-11.50^\circ$ versus $41.31+/-8.86^\circ$; $p<0.05$) and decreased, albeit not significantly, with age at a rate of $+/-2^\circ$ every decade. For lateral bending and axial rotation, no correlation of global ROM with age was seen. No significant differences were seen in CTM or in translation during flexion/extension and lateral bending ($p>0.05$). However, significant intergroup differences were seen in craniocaudal translation and CTM ($p<0.05$) between groups I and III versus II and IV during axial rotation. No intergroup differences in COR were observed during flexion/extension and lateral bending ($p>0.05$). ROM and translation were significantly correlated during flexion/extension and lateral bending (Spearman $r>0.4$; $p<0.05$). A significant intergroup difference in intervertebral disc degeneration was found between groups I and II versus III and IV ($p<0.05$). Intervertebral ROM during flexion/extension and lateral bending was significantly correlated with intervertebral disc degeneration (Spearman r -0.13 and -0.17, $p<0.05$). Intervertebral ROM at a level adjacent to a severely degenerated level (degeneration score ≥ 7) was 4.9% higher during flexion/extension, 1.4% during lateral bending and 1.3% during axial rotation on average, compared to intervertebral ROM at a level adjacent to a level free of degeneration (degeneration score = 0).

Conclusions Age has no predominant effect on the quantity or quality of intervertebral motion during flexion/extension, lateral bending or axial rotation. Intervertebral disc degeneration increases according to age, especially

at C5-C6 and C6-C7. A more degenerated spinal unit tends to have reduced mobility in asymptomatic individuals during flexion/extension and lateral bending. Levels adjacent to a severely degenerated level tend to compensate the loss of motion.

5.1 Introduction

Many studies have reported on normal motion patterns of the cervical spine during flexion and extension. Most of these studies used plain radiographs of the cervical spine in full flexion and full extension positions to determine the intervertebral range of motion (ROM) in the sagittal plane [8, 10, 16, 21, 27, 28, 29]. Reitman et al. used fluoroscopy to extract full flexion and full extension images from a video sequence [34]. Others used lateral fluoroscopy to measure continuous angular motion (CAM) in function of the percentage of the motion cycle or in function of the number of frames [15, 46, 48, 23, 47] in order to assess the quality of motion.
In contrast to motion patterns in the sagittal plane, i.e. flexion and extension, intervertebral motion in the coronal and axial plane, i.e. lateral bending and axial rotation, are rarely studied.
So far, no studies have reported on normal CAM or continuous translational motion (CTM) in function of the motion cycle or in function of the number of frames during lateral bending or axial rotation. The identification of these continuous motion patterns might provide further insight in the kinematic behavior of the cervical spine and can be used as input for the development of arthroplasty devices as well as to determine whether or not it make sense to use such devices.

Few studies have investigated the effect of cervical disc degeneration on intervertebral motion [41, 25, 26]. Simpson et al. [40] evaluated flexion and extension motion and used the Kellgren scoring system [20] based on lateral radiographs to grade cervical disc degeneration at each level. Miyazaki et al. and Morishita et al. [25, 26] used MRI obtained in flexion and extension positions to calculate the lateral motion patterns. They scored all intervertebral discs for degeneration by a previously reported grading system using MRI. The effect of disc degeneration on lateral bending and axial rotation has not been studied up to date.

The purpose of this study was to establish a database of quantitative and qualitative motion patterns during flexion to extension, left to right lateral bending and left to right axial rotation of asymptomatic volunteers of different ages with different degrees of disc degeneration using fluoroscopy. Next to these motion patterns, degeneration of the intervertebral disc was assessed in order to possibly correlate the degree of degeneration with motion of the cervical spine.

5.2 Materials and methods

5.2.1 Study design and set-up

Fluoroscopic images were obtained from 60 asymptomatic Caucasian volunteers equally divided over 4 age groups: group I (18-30 years), group II (31-40 years), group III (41-50 years) and group IV (51-60 years).
Two perpendicularly oriented fluoroscopic cameras were used for acquisition of the fluoroscopic image sequences. The center of the field of view of each camera was focused on the center of the vertebral body of C5. The pulse frequency was 3 Hz. The tube voltage and tube current were 50 kV and 0.5 mA, resulting in an average patient dose of 0.1 mSv.
Volunteers with a history of neck pain, previous neck trauma or neck surgery, and pregnant or breastfeeding women were excluded from this study.
Before the movement was recorded, the volunteers were coached to maximally flex and extend, bend and rotate their neck and to prevent out-of-plane movement. Each movement was performed within a 6 to 8-second period. A led skirt was provided to protect the lower body. During the measurements, the volunteer sat on a chair with a lumbar support and the knees flexed at 90°. To increase visibility of C7 by lowering the shoulders and to avoid interference of thoracic movement, the volunteers were asked to grasp the back ends of the chair.
This study obtained approval from the Radioprotection Department and the Ethics Committee (UZ Gasthuisberg, Leuven, Belgium). All volunteers signed an informed consent.

5.2.2 Measurements

Motion patterns were characterized using four qualitative and three quantitative parameters. Global continuous angular motion (CAM) is defined as the rotation of C3 with respect to C6 and is expressed in degrees (e.g. figure 5.1). Intervertebral CAM is defined as the rotation of a cranial vertebra with respect to its caudal vertebra. Because volunteers move with different speeds during the acquisition, intervertebral CAM is expressed in function of global angular motion, similar to the approach of Wu et al. [46]. Intervertebral CTM is defined as the translation of a cranial vertebra with respect to its caudal vertebra and was defined as the translation of the geometric center of the cranial vertebral body along an axis parallel to the cranial endplate of the caudal vertebral body. Anteroposterior (AP) translation was calculated during flexion/extension. Lateral (LAT) translation was calculated during lateral bending. Craniocaudal (CC) translation was calculated during axial rotation. Translation was normalized to the width of the vertebral body [10] to cope with magnification of the radiographs. As last qualitative parameter, the location of the center of rotation is calculated during flexion/extension and lateral bending. Next, three quantitative parameters were calculated. Global ROM is calculated as the difference between maximum and minimum global CAM (figure 5.1). Likewise, intervertebral ROM is the difference between maximum and minimum intervertebral CAM and intervertebral AP, LAT and CC translation is the difference between the maximal and minimal AP, LAT and CC CTM for each intervertebral level (figure 5.1). These differences are measures for the amount of global and intervertebral motion. All parameters were calculated during flexion to extension, left to right lateral bending and left to right axial rotation. Flexion/extension motion patterns were assessed based on a lateral image sequence and were calculated using a custom developed semi-automatic motion analysis tool (e.g. figure 5.1). This tool has an excellent repeatability (intraclass correlation coefficient [39]>0.77) and a low measurement error [3] (0.3° and 0.4 mm) (Walraevens et al., unpublished data). Lateral bending motion patterns were assessed based on an AP image sequence and were calculated by manually identifying four identical anatomical landmarks on each frame (e.g. figure 5.2). Those landmarks were tracked using a planar iterative closest point algorithm [2]. The intraclass correlation coefficient and measurement errors of this method were 0.5 and 1.33° and 1.8 mm respectively. Axial rotation motion patterns were assessed based on simultaneous acquired AP and lateral image sequences and were calculated by manually identifying five identical anatomical landmarks on each lateral and AP frame of the image sequences. Based on these five landmarks a three dimensional pyramidal virtual shape of the vertebra was reconstructed (figure 5.3). Using an iterative closest point algorithm [2], the virtual shapes of the vertebrae were aligned between the different frames. The intraclass correlation coefficient and measurement errors of this method were 0.97 and 0.88° and 1.2 mm respectively.

Prior to the identification and tracking of the anatomical landmarks, geometric distortion caused by the image intensifier was minimized using a correction matrix. To obtain this matrix, an X-ray image of a calibration grid was taken for both fluoroscopic cameras. From this image, based on the prior knowledge of the grid, the correction matrix was calculated by mapping the original pixel coordinates to the corrected pixel.

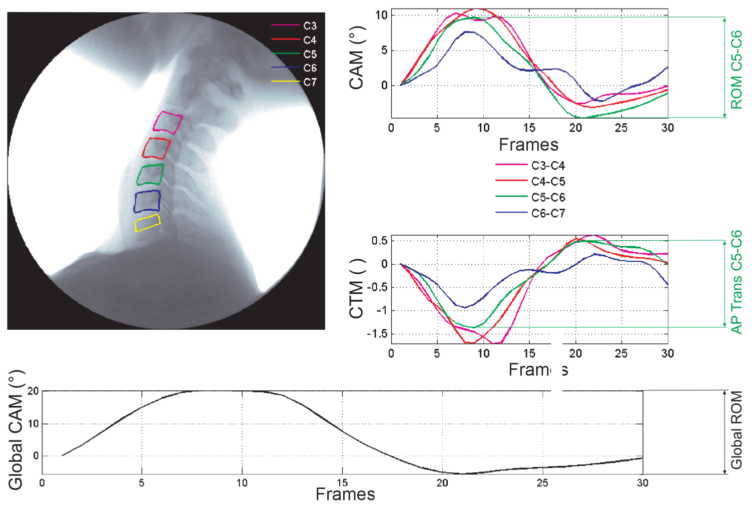

Figure 5.1: Intervertebral continuous angular motion (CAM), continuous translational motion (CTM) and global CAM (C3-C6) during flexion/extension. Frame 0: neutral position, frame 9: full flexion position, frame 21: full extension position, frame 30: neutral position. Range of motion (ROM) and AP translation of C5-C6 is calculated as the difference between the maximum CAM respectively CTM during full flexion (frame 9) and minimum CAM respectively CTM during full extension (frame 21). Likewise, global ROM is calculated as the difference between the maximum and minimum global CAM.

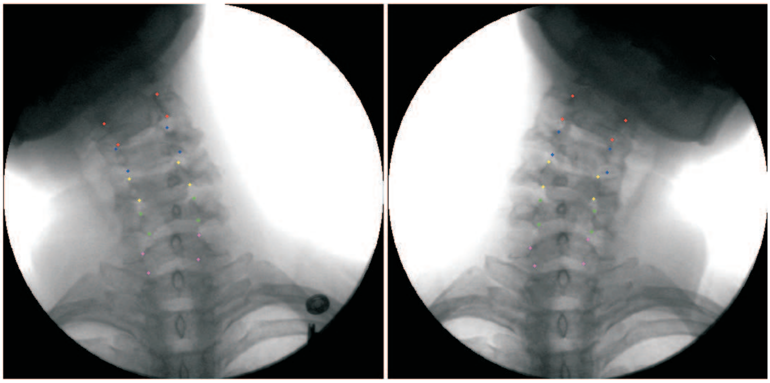

Figure 5.2: Anatomical landmarks identified on two frames of an AP image sequences during lateral bending.

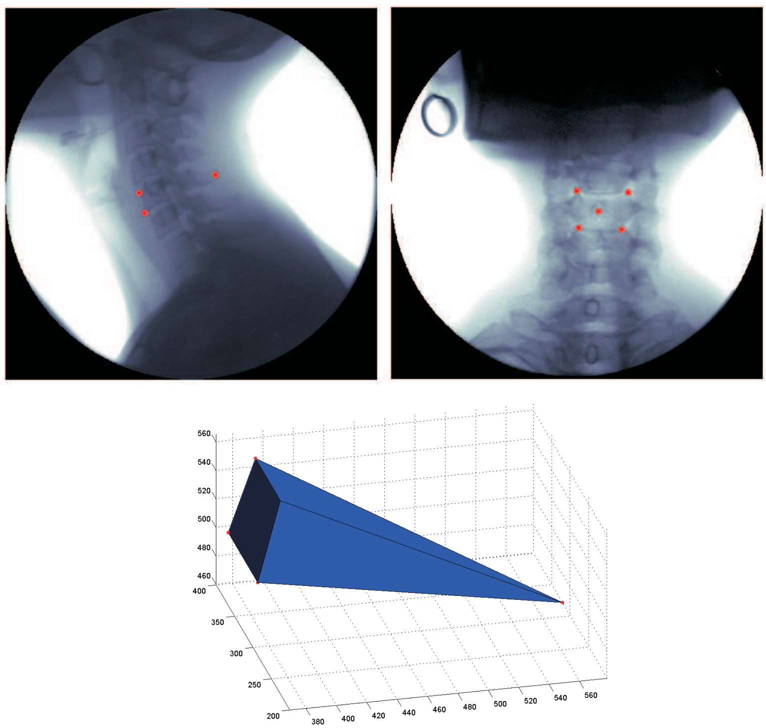

Figure 5.3: Anatomical landmarks identified on two simultaneous acquired frames of lateral (left) and AP (right) image sequences during axial rotation and the 3D pyramidal reconstruction of the vertebra (bottom).

Intervertebral disc degeneration was assessed using a validated, objective and quantitative scoring system [43]. On lateral radiographs, the overall degeneration score is calculated based on three variables: height loss, anterior osteophytes and endplate sclerosis (table 5.1). Each variable contributes with decreasing importance to the total degeneration score. The overall score ranges from 0 (no degeneration) to 9 (severe degeneration).

Table 5.1: Scoring system of cervical disc degeneration based on neutral lateral radiographs [44].

1. Height loss†	0%	0 points
Middle disc height compared	$\leq$25%	1 points
to normal middle disc height	>25% - $\leq$50%	2 points
at an adjacent level	>50% - $\leq$75%	3 points
	>75%	4 points
2. Anterior osteophytes	No osteophytes	0 points
with respect to the AP diameter	$\leq$ 1/8 AP diameter	1 point
of the corresponding VB	> 1/8 - $\leq$ 1/4 AP diameter	2 points
	> 1/4 AP diameter	3 points
3. Endplate sclerosis	No sclerosis	0 points
	Detectable	1 point
	Definite	2 points
Overall degree of disc degeneration	0 points (no degeneration)	
= 1 + 2 + 3	1-3 points (mild degeneration)	
	4-6 points (moderate degeneration)	
	7-9 points (severe degeneration)	

5.2.3 Statistical analysis

A p-value of 0.05 was considered significant. Linear correlations were investigated using the Spearman r correlation coefficient. A Student t-test was used to compare both groups if the data was Gaussian and continuous. In other situations, a Mann-Whitney U-test was used.

5.3 Results

5.3.1 Demographics

Table 5.2 provides a summary of the volunteer demographic data. The mean age of group I was 25.5 years; the mean age of group II was 34.8 years; the mean age of group III was 45.4 years; and the mean age of group IV was 55.1 years old. In total, there were 40 male and 20 female volunteers. The ratio male to female volunteers was 10 to 5 for group I, 12 to 3 for group II, 11 to 4 for group III, and 8 to 7 for group IV.

Table 5.2: Summary of the asymptomatic volunteer demographics. Mean +/- standard deviation (range).

	Number	Age (yrs)	Weight (kg)	Length (m)
Total	60	40.2 +/- 11.6 (23-60)	74.8+/-12.5	1.77+/-0.08
Female	20	42.4 +/- 12.6 (23-60)	66.2+/-11.7	1.68+/-0.04
Male	40	39.1 +/- 11.1 (23-60)	79.1+/-10.6	1.81+/-0.05
Age group I (18-30y)	15	25.5 +/- 2.3 (23-29)	71.1+/-10.7	1.78+/-0.08
Age group II (31-40y)	15	34.8 +/- 3.3 (31-40)	74.6+/-8.7	1.77+/-0.06
Age group III (41-50y)	15	45.4 +/- 3.1 (41-50)	79.5+/-15.3	1.76+/-0.09
Age group IV (51-60y)	15	55.1 +/- 2.9 (51-60)	74.1+/-14.0	1.75+/-0.09

5.3.2 Flexion/extension motion patterns

As shown in table 5.3 there is no significant difference in intervertebral ROM or in AP translation between the age groups, with exception of a significant difference in ROM between group I and II at C6-C7 (11.89+/-4.94° versus 15.60+/-4.04°; $p<0.05$). Global ROM decreases nonsignificantly with age at a rate of +/-2° every decade. A significant difference in global ROM is observed between group I and group IV (48.64+/-11.50° versus 41.31+/-8.86°; $p<0.05$). Intervertebral ROM was significantly positively correlated with AP translation in all groups individually. Spearman r correlation coefficients were 0.698, 0.651, 0.639, and 0.569 for groups I, II, III and IV respectively ($p<0.05$).
When intervertebral CAM and AP CTM during flexion to extension is examined in function of global CAM, figures 5.4 and 5.5 show no large intergroup differences for all levels except for level C6-C7. Figure 5.4 reveals that flexion/extension motion was initiated at C3-C4 and C4-C5 for all groups. For group III and IV, a negative contribution of C6-C7 at the initial phase of flexion/extension can be observed.

Table 5.3: Intervertebral and global (gbl) range of motion (ROM) and translation (TR) during flexion/extension, lateral bending and axial rotation for four age groups and all volunteers. Mean +/- standard deviation. †Average intragroup ROM for all intervertebral levels. ^{X}significant difference with respect to group X (p<0.05). AP: anteroposterior, LAT: lateral, CC: craniocaudal.

	Group I	Group II	Group III	Group IV	All
Flexion/extension					
glb ROM C3-C6 (°)	48.6+/-11.5^{IV}	46.5+/-14.0	44.3+/-10.4	41.1+/-8.9^{I}	45.2+/-11.4
ROM C3-C4 (°)	16.6+/-4.5	14.3+/-4.8	15.8+/-4.7	16.3+/-4.0	15.7+/-4.5
ROM C4-C5 (°)	18.1+/-4.8	16.9+/-7.0	15.2+/-5.4	14.7+/-5.0	16.2+/-5.6
ROM C5-C6 (°)	16.4+/-4.7	18.0+/-5.2	15.7+/-3.5	14.2+/-6.0	16.1+/-5.0
ROM C6-C7 (°)	11.9+/-4.9^{II}	15.6+/-4.0^{I}	11.9+/-5.0	12.2+/-5.1	12.00+/-4.9
ROM† (°)	15.8+/-5.2	16.2+/-5.5	14.9+/-4.7	14.6+/-5.1	15.4+/-5.1
AP TR C3-C4 (/)	0.27+/-0.09	0.24+/-0.11	0.27+/-0.08	0.24+/-0.09	0.25+/-0.19
AP TR C4-C5 (/)	0.30+/-0.11	0.27+/-0.11	0.31+/-0.07	0.26+/-0.09	0.28+/-0.19
AP TR C5-C6 (/)	0.27+/-0.08	0.23+/-0.08	0.26+/-0.09	0.22+/-0.13	0.24+/-0.19
AP TR C6-C7 (/)	0.14+/-0.05	0.18+/-0.06	0.17+/-0.08	0.15+/-0.08	0.16+/-0.14
AP TR† (/)	0.25+/-0.17	0.23+/-0.19	0.25+/-0.16	0.21+/-0.20	0.23+/-0.36
Lateral bending					
glb ROM C3-C6 (°)	23.8+/-5.2	22.5+/-7.8	22.0+/-8.9	24.7+/-6.5	23.4+/-7.0
ROM C3-C4 (°)	8.0+/-4.9	11.0+/-5.2	8.3+/-4.7	9.4+/-2.9	9.1+/-4.3
ROM C4-C5 (°)	7.6+/-4.7	7.3+/-3.5	7.2+/-4.3	8.6+/-4.2	7.7+/-4.2
ROM C5-C6 (°)	7.7+/-3.2	5.2+/-3.1	7.4+/-3.3	6.8+/-2.5	6.9+/-3.1
ROM C6-C7 (°)	8.8+/-3.6	8.5+/-4.2	11.5+/-5.2	8.0+/-3.8	9.2+/-4.3
ROM† (°)	8.1+/-4.0	7.9+/-4.4	8.5+/-4.6	8.2+/-3.5	8.2+/-4.1
LAT TR C3-C4 (/)	0.16+/-0.07	0.16+/-0.08	0.17+/-0.06	0.19+/-0.09	0.17+/-0.15
LAT TR C4-C5 (/)	0.20+/-0.07	0.18+/-0.08	0.22+/-0.05	0.18+/-0.08	0.19+/-0.14
LAT TR C5-C6 (/)	0.16+/-0.06	0.16+/-0.06	0.20+/-0.12	0.20+/-0.12	0.18+/-0.19
LAT TR C6-C7 (/)	0.08+/-0.04	0.12+/-0.05	0.11+/-0.06	0.11+/-0.07	0.11+/-0.11
LAT TR†(/)	0.15+/-0.12	0.15+/-0.13	0.17+/-0.15	0.17+/-0.18	0.16+/-0.30
Axial rotation					
glb ROM C3-C6 (°)	19.9+/-8.2^{II}	30.7+/-7.8^{I}	30.4+/-14.3	24.0+/-7.2	24.9+/-11.1
ROM C3-C4 (°)	7.9+/-4.2	11.6+/-3.7	12.3+/-7.7	10.0+/-2.8	10.3+/-3.6
ROM C4-C5 (°)	8.8+/-4.6	11.0+/-3.0	9.4+/-4.9	7.7+/-3.4	9.2+/-4.0
ROM C5-C6 (°)	5.5+/-3.1	6.3+/-3.3	8.3+/-4.6	8.0+/-2.9	7.0+/-3.6
ROM C6-C7 (°)	3.4+/-2.9	4.4+/-2.7	6.1+/-4.3	6.0+/-3.3	4.8+/-3.2
ROM† (°)	6.1+/-4.1	7.6+/-3.9	8.2+/-4.8	7.7+/-3.2	7.3+/-4.0
CC TR C3-C4 (/)	0.06+/-0.03	0.08+/-0.04	0.07+/-0.03	0.08+/-0.03	0.07+/-0.03
CC TR C4-C5 (/)	0.06+/-0.03^{II}	0.09+/-0.04^{I}	0.07+/-0.04	0.08+/-0.04	0.07+/-0.04
CC TR C5-C6 (/)	0.05+/-0.04^{II,IV}	0.09+/-0.04^{I,III}	0.05+/-0.03^{II,IV}	0.09+/-0.05^{I,III}	0.07+/-0.04
CC TR C6-C7 (/)	0.05+/-0.03	0.08+/-0.05	0.07+/-0.05	0.05+/-0.03	0.07+/-0.04
CC TR†(/)	0.06+/-0.06	0.09+/-0.08	0.06+/-0.08	0.08+/-0.08	0.08+/-0.08

The CORs did not differ significantly between the age groups at all intervertebral levels (figure 5.9; p<0.05).

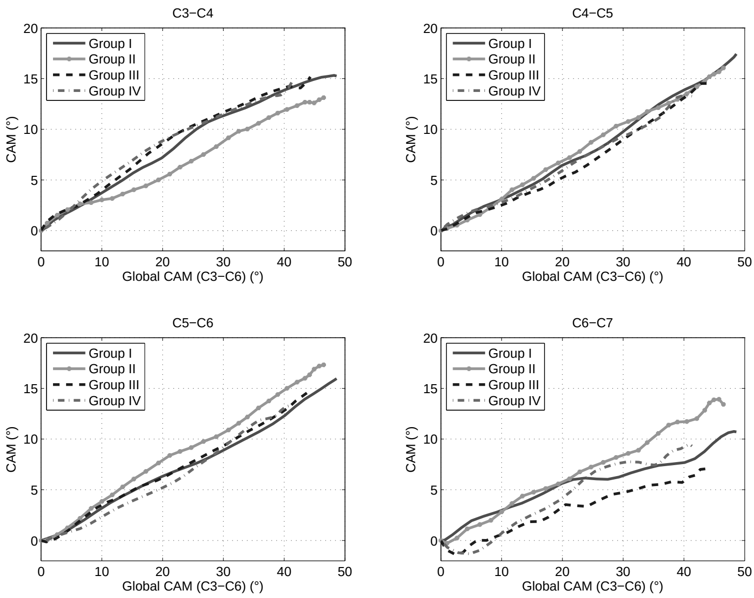

Figure 5.4: Intergroup comparison of group-averaged intervertebral continuous angular motion (CAM) in lateral projection during flexion/extension in function of global CAM (C3-C6) for intervertebral levels C3-C4 to C6-C7.

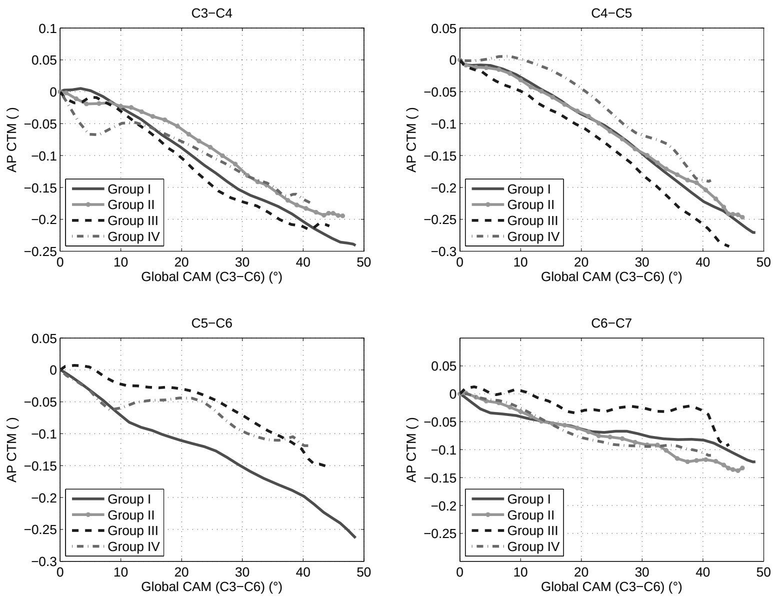

Figure 5.5: Intergroup comparison of group-averaged intervertebral anteroposterior (AP) continuous translational motion (CTM) in lateral projection during flexion/extension in function of global CAM (C3-C6) for intervertebral levels C3-C4 to C6-C7.

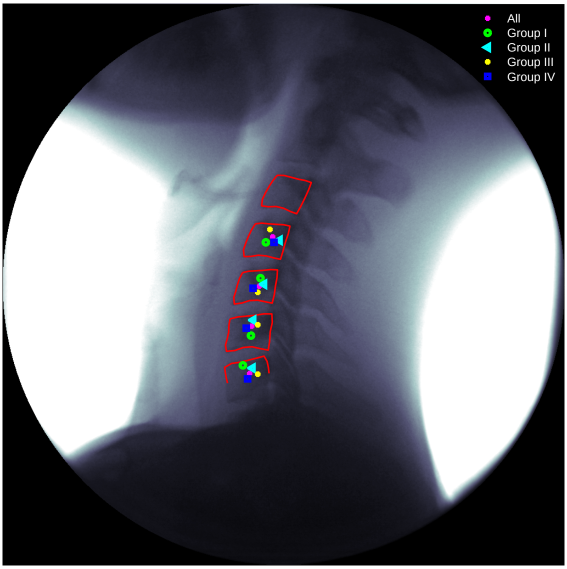

Figure 5.6: Intergroup comparison of group-averaged center of rotation (COR) in lateral projection during flexion/extension for intervertebral levels C3-C4 to C6-C7. Magenta dot: all volunteers, green circle: group I, cyan triangle: group II, yellow dot: group III, blue square: group IV.

5.3.3 Lateral bending motion patterns

As shown in table 5.3, there is no significant difference in intervertebral ROM or in lateral translation between the age groups for lateral bending. No correlation of global ROM with age is observed ($p>0.05$). Intervertebral ROM was significantly positively correlated with lateral translation in all groups individually. Spearman r correlation coefficients were 0.436, 0.560, 0.480, and 0.456 for groups I, II, III and IV respectively ($p<0.05$).
When intervertebral CAM and lateral CTM during left to right lateral bending is analyzed in function of global CAM, figures 5.7 and 5.8 shows no significant intergroup differences for all levels except for level C3-C4 of CAM of group II with respect to the other groups. For all groups motion was initiated at C3-C4 and C4-C5.
The CORs did not differ significantly between the age groups at all intervertebral levels (figure 5.9; $p<0.05$).

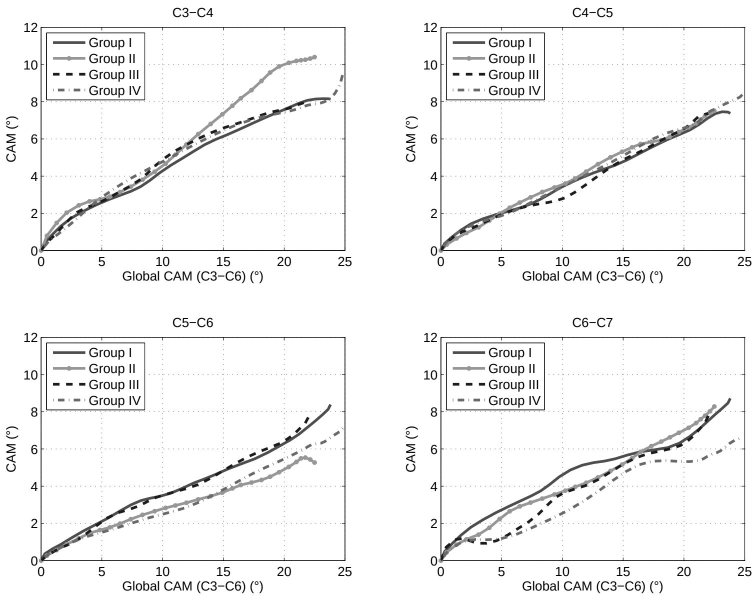

Figure 5.7: Intergroup comparison of group-averaged intervertebral continuous angular motion (CAM) in coronal projection during left to right lateral bending in function of global CAM (C3-C6) for intervertebral levels C3-C4 to C6-C7

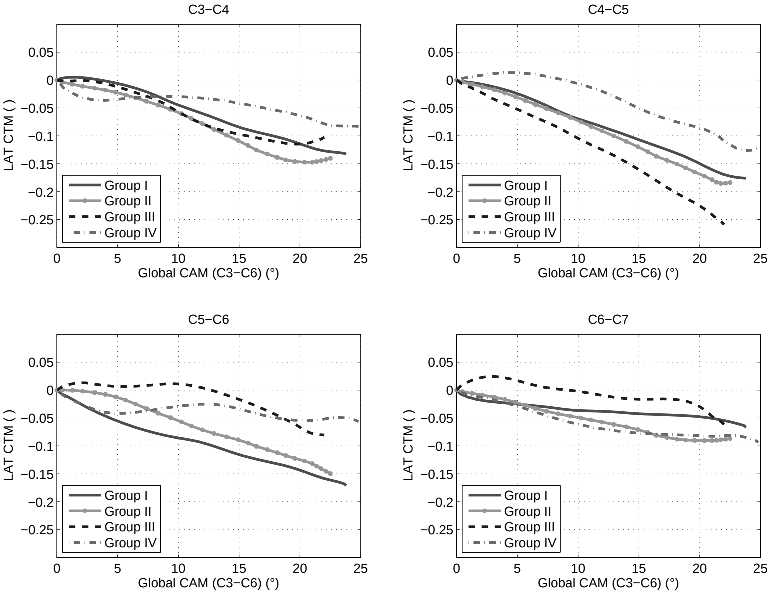

Figure 5.8: Intergroup comparison of group-averaged intervertebral lateral (LAT) continuous translational motion (CTM) in coronal projection during flexion to extension in function of global CAM (C3-C6) for intervertebral levels C3-C4 to C6-C7.

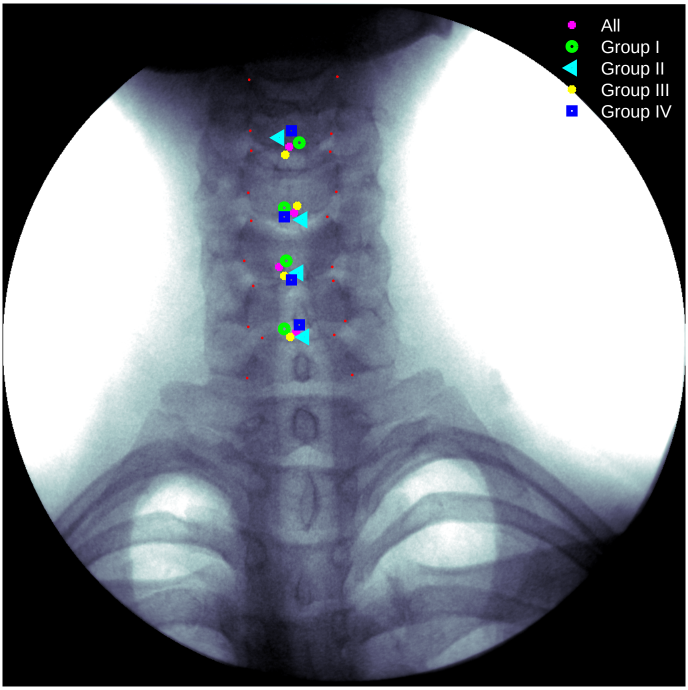

Figure 5.9: Intergroup comparison of group-averaged center of rotation (COR) in coronal projection during lateral bending for intervertebral levels C3-C4 to C6-C7. Magenta dot: all volunteers, green circle: group I, cyan triangle: group II, yellow dot: group III, blue square: group IV.

5.3.4 Axial rotation motion patterns

As shown in table 5.3, there is no significant difference in intervertebral ROM between the age groups for axial rotation. However there are significant intragroup differences when comparing the ROM of C3-C4 with the ROM of C6-C7 for all groups, the former being more mobile. As a general trend, the intervertebral levels C3-C4 and C4-C5 have a larger ROM than the more caudal levels. Global ROM of group I differed significantly from group II (19.9+/-8.2° versus 30.7+/-7.8°; $p<0.05$). CC translation of C4-C5 differed significantly between groups I and IV ($p<0.05$). Moreover, at C5-C5, CC translation of groups I and III was significantly different compared to groups II and IV ($p<0.05$), the latter groups having larger CC translations. In contrast to flexion/extension and lateral bending, intervertebral ROM during axial rotation was not significantly correlated with CC translation ($p>0.05$).
When intervertebral CAM during left to right axial rotation is studied in function of global CAM, figure 5.11 shows no significant intergroup differences for all levels. Motion was initiated at C3-C4 and C4-C5 for all groups.

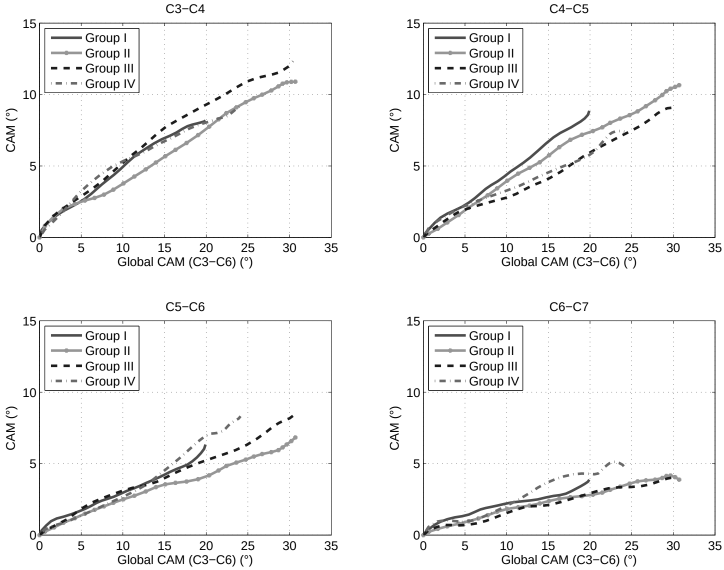

Figure 5.10: Intergroup comparison of group-averaged intervertebral continuous angular motion (CAM) in axial projection during left to right axial rotation in function of global angular CAM (C3-C6) for intervertebral levels C3-C4 to C6-C7

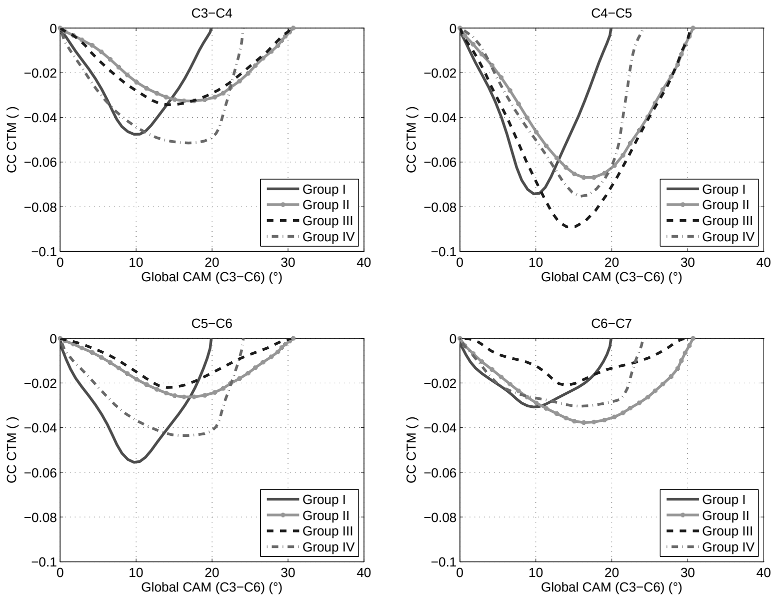

Figure 5.11: Intergroup comparison of group-averaged intervertebral craniocaudal (CC) continuous translation motion (CTM) in axial projection during left to right axial rotation in function of global angular CAM (C3-C6) for intervertebral levels C3-C4 to C6-C7

5.3.5 Intervertebral disc degeneration

Within groups III and IV, levels C3-C4 and C4-C5 show a significant difference in degeneration score with respect to levels C5-C6 and C6-C7, the latter being more degenerated ($p<0.05$; table 5.4). A significant intergroup difference in intervertebral disc degeneration is found between groups I and II versus III and IV ($p<0.05$; table 5.4).
A significant correlation between flexion/extension and lateral bending intervertebral ROM and intervertebral disc degeneration is found (Spearman $r =$ -0.13 and -0.17, $p<0.05$). For flexion/extension, every increase by 1 point in the degeneration score results in a ROM decrease of 0.5° with respect to the average intervertebral ROM at a non-degenerated level. Likewise, for lateral bending, every increase by 1 point in the degeneration score results in a ROM decrease of 0.6° with respect to the average intervertebral ROM at a non-degenerated level. For axial rotation, intervertebral ROM and disc degeneration are not

significantly correlated (r= -0.05; p>0.05).
Intervertebral ROM at a level adjacent to a severely degenerated level (degeneration score ≥7) is 4.9% higher during flexion/extension, 1.4% during lateral bending and 1.3% during axial rotation on average, compared to intervertebral ROM at a level adjacent to a level free of degeneration (degeneration score=0).
Furthermore, intervertebral AP and lateral translation during flexion/extension and lateral bending are significantly negatively correlated with intervertebral disc degeneration (Spearman r = -0.23 and -0.19, p<0.05).

Table 5.4: Comparison of intervertebral degeneration of different age groups based on the 9 point scale scoring system by Walraevens et al. [43]. †Average disc degeneration score for all levels. ^{X}Significant difference with respect to group X (p<0.05).

	Group I	Group II	Group III	Group IV	All
Degeneration C3-C4	0.07+/-0.26	0.07+/-0.26	0.27+/-0.46	0.20+/-0.56	0.15+/-0.40
Degeneration C4-C5	0.20+/-0.41	0.27+/-0.46	0.20+/-0.41	0.40+/-0.63	0.27+/-0.48
Degeneration C5-C6	1.20+/-1.57	1.13+/-1.81	0.80+/-0.94	1.67+/-1.88	1.20+/-1.58
Degeneration C6-C7	1.15+/-2.23	1.00+/-1.13	0.80+/-0.86	1.33+/-1.91	1.07+/-1.58
Degeneration All†	0.25+/-0.51^{III,IV}	0.23+/-0.53^{III,IV}	0.83+/-1.10^{I,II}	1.42+/-1.89^{I,II}	0.68+/-1.24

5.4 Discussion

The purpose of this study was to establish a database of quantitative and qualitative motion patterns during flexion/extension, left to right lateral bending and left to right axial rotation of asymptomatic volunteers of different ages with different degrees of disc degeneration using fluoroscopy. From these image sequences, global and intervertebral motion patterns in the different planes were calculated. In addition, degeneration of the intervertebral disc was assessed in order to correlate the degree of degeneration with motion of the cervical spine.

The semi-automatic motion tool used to calculate lateral intervertebral motion patterns is based on a generic model-based segmentation algorithm developed at Medical Image Computing (Radiology-ESAT/PSI, KULeuven, Belgium) [38]. It has an excellent repeatability (intraclass correlation coefficient [39]>0.77) and a low measurement error [3] (0.3° and 0.4 mm) (Walraevens et al., unpublished data). The accuracy is comparable to that of the QMA software by Medical Metrics Inc. (USA) which has proven its value in

numerous studies [34, 32, 14, 35, 36]. Excellent intra-rater agreement and a low measurement error are also found for the axial rotation method. In contrast, a fair intra-rater agreement for lateral bending was observed. This discrepancy may be explained by the fact that the lateral bending method is solely based on an AP image sequence instead of biplanar image sequences like we used for axial rotation. For this study, the use of biplanar image sequences was limited to avoid an excessive exposure to radiation for asymptomatic volunteers. This method assumes therefore no out of plane motion for the calculation of the motion patterns. However, out of plane motion does occur during both lateral bending and axial rotation due to the anatomy of the facet and uncovertebral joints [4, 17, 24, 18, 19]. Cook et al. presented an overview of the coupling behavior of the cervical spine [7] and concluded that axial rotation occurs simultaneously to the same side under lateral bending at levels C2-C3 and caudal and visa versa. As biplanar image sequences were available for axial rotation, the axial rotation method can cope with out of plane motion resulting in the lower measurement error and higher intra-rater agreement.
The ROM results for flexion/extension, lateral bending and axial rotation lay within the broad range of ROM values previously reported in literature (see figures 5.12, 5.13 and 5.14). No general intergroup differences or trends in intervertebral ROM could be found, indicating that age has no predominant effect on intervertebral ROM in the different planes for the study population. This is consistent with the findings of Reitman et al. [34] for flexion/extension intervertebral ROM. Our results show a significant higher ROM in group II compared to group I. This might be explained by the fact that two volunteers of group II had a ROM at C6-C7 which exceeded 19°. We did not classify those patients as outliers as literature data suggest that ROMs at C6-C7 greater than 20° sometimes occur [46, 45]. If these patients were to be omitted from group II, ROM of this group would not significantly differ from the other groups.
Flexion/extension global ROM tended to decrease with age, albeit not significantly, at a rate of +/-2° every decade. This observation is consistent with the results found by Dvorak et al. and Gore et al. [8, 13]. This is however lower than the value of about 4° per decade reported by Chen et al. [5] and 5° per decade by Simpson et al. [40]. In the aforementioned studies, global ROM was defined as the angular displacement of the head and entire cervical spine as a single unit of motion [8, 5, 13]. Both for lateral bending and for axial rotation, no relation between intervertebral global ROM and age was observed.

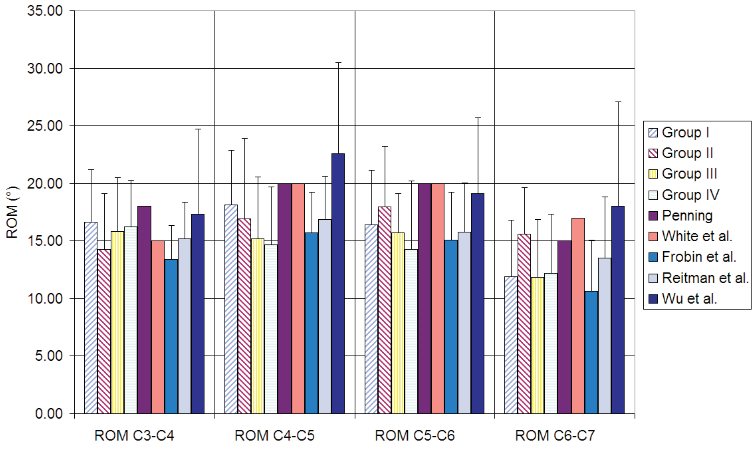

Figure 5.12: Intervertebral range of motion (ROM) in lateral projection during flexion/extension of 4 age groups of asymptomatic volunteers (group I: 18-30 yrs, group II: 31-40 yrs, group III: 41-50 yrs, group IV: 51-60 yrs) versus previously reported values of Penning [28], White et al. [45], Frobin et al. [10], Reitman et al. [34] and Wu et al. [46].

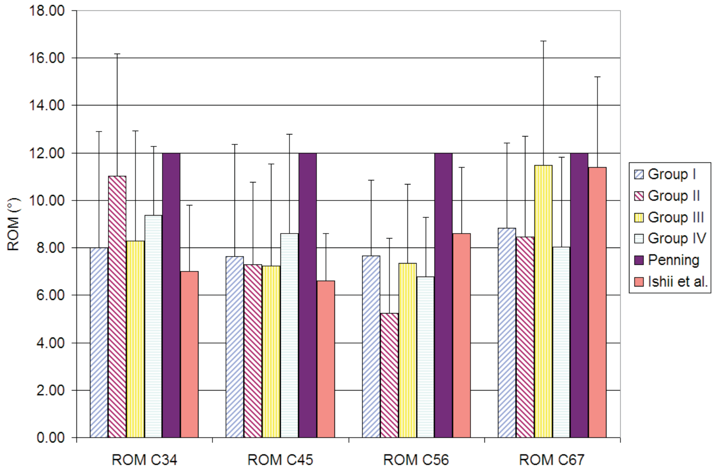

Figure 5.13: Intervertebral range of motion (ROM) in anteroposterior projection during left to right lateral bending of 4 age groups of asymptomatic volunteers (group I: 18-30 yrs, group II: 31-40 yrs, group III: 41-50 yrs, group IV: 51-60 yrs) versus previously reported values of Penning [28] and Ishii et al. [18].

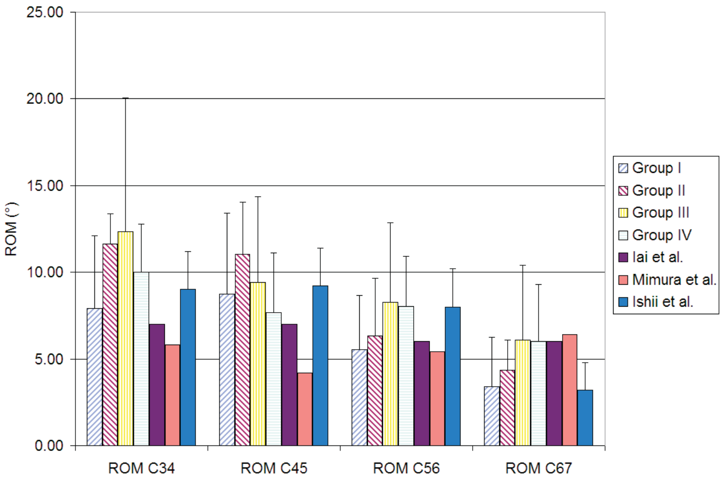

Figure 5.14: Intervertebral range of motion (ROM) in axial projection during left to right axial rotation of 4 age groups of asymptomatic volunteers (group I: 18-30 yrs, group II: 31-40 yrs, group III: 41-50 yrs, group IV: 51-60 yrs) versus previously reported values of Penning [28], Iai et al. [17], Mimura et al. [24] and Ishii et al. [19].

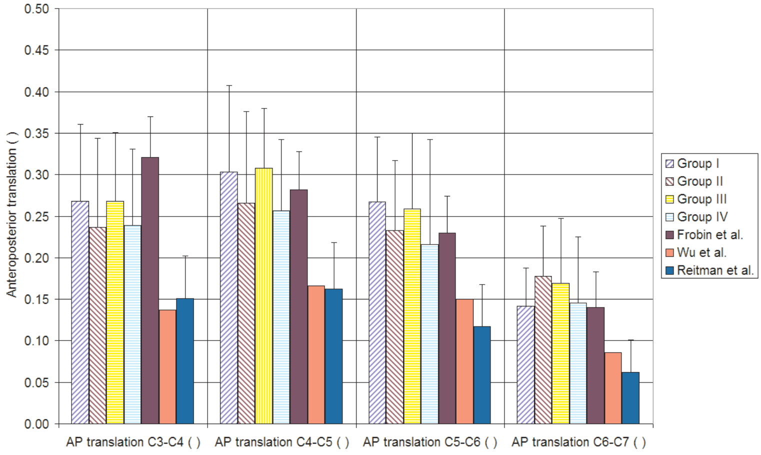

Figure 5.15: Intervertebral anteroposterior (AP) translation in lateral projection during flexion/extension of 4 age groups of asymptomatic volunteers (group I: 18-30 yrs, group II: 31-40 yrs, group III: 41-50 yrs, group IV: 51-60 yrs) versus previously reported values of Frobin et al. [10], Reitman et al. [34] and Wu et al. [46].

The AP translation results for flexion/extension lay within the broad range of ROM values previously reported in literature (see figure 5.15). No literature data on lateral translation during lateral bending and CC translation during axial rotation was found. CC translation during axial rotation differed significantly between the age groups for several intervertebral levels. The differences might however be explained by the fact that the measured translations were in the same order of magnitude as the measurement error. CC and LAT translation results should therefore be interpreted with caution. To summarize, no general intergroup differences or trends in intervertebral translation could be found, indicating that age has no predominant effect on intervertebral translation in the different planes.
It is difficult to compare intervertebral continuous angular motion (CAM) during flexion/extension in function of global angular motion with historical results, as only few of them are available in literature today. Only Van Mameren et al., Goffin et al. and Wu et al. reported reliable data [46, 48, 38, 47, 6, 11]. Similar to Van Mameren et al. it was observed that the minimum in CAM for certain intervertebral levels, particularly C6-C7, does not necessarily co-appears with minimal global CAM [23]. This confirms the statements that global ROM is not the arithmetic sum of its intervertebral ROMs [4]. It also explains why an age dependency with global ROM and not with intervertebral ROM is possible during flexion/extension. A historical comparison of CAM or CTM during left to right lateral bending and axial rotation in function of global angular motion is not possible as no data is available in literature up to date. Similar to motion during flexion/extension, motion is initiated at C3-C4 and C4-C5 during left to right lateral bending for all groups. The significant higher intervertebral CAM during lateral bending of group II compared to the other groups might be explained by the influence of one volunteer of group II who appeared to have hypermobility at C3-C4. If this patient was to be omitted from group II, CAM of this group would not significantly differ from the other groups. The influence of this patient on the flexion/extension and axial rotation results of C3-C4 was negligible. As mentioned earlier, the intergroup differences in CC CTM during axial rotation might be explained by the fact that the measured translations were of the same order of magnitude as the measurement error. They should therefore be interpreted with caution.
The CORs during flexion/extension are similar to the previous reported locations [1, 4, 9, 42]. Similarly, the locations of the CORs at lower cervical levels were situated close to the intervertebral disc and close to the middle of the superior endplate. However, the hypothesis that the location of the COR of higher cervical levels is more caudally and posteriorly was not substantiated in this research. A historical comparison with CORs during lateral bending is difficult as no reliable data is available in literature up to date. During lateral bending, the COR were situated slightly cranially of the intervertebral

disc and on the midline, probably due to the saddle shape of the cervical uncovertebral joints [4]. This is in contrast to the location of the COR during flexion/extension, where the CORs are situated caudally of the intervertebral. This discrepancy has an important impact on the design considerations for cervical disc prosthesis, and has caused a ball-and-socket design with the ball pointed upward, e.g. Porous Coated Motion (CerviTech) and the Prodisc-C (Synthes), as well as ball-and-socket or ball-and-trough designs with the ball pointed downward, e.g. Prestige (Medtronic). Ideally, prostheses should be able to mimic a caudally located COR during flexion/extension and a cranially located COR during lateral bending. Mobile-core or non-constrained prostheses, such as the the Bryan Cervical Disc prosthesis (Medtronic) and saddle-shaped prostheses, such as the Altia TDI (Amedica) and CerviCore (Stryker) aim to provide this possibility.
The locations of the COR during axial rotation were not analyzed at this stage. This is a goal for future research.
A clear age related trend in intervertebral disc degeneration can be observed. Degeneration increases with age, with significant increases at levels C5-C6 and C6-C7. These are the levels that are most frequently operated upon for intervertebral disc disease [12, 14]. Literature suggests that the larger mobility of the lower levels, especially C5-C6, might be the reason for this marked difference in degeneration [25, 26]. Our results did not confirm this hypothesis as none of the groups had a significant greater mobility at C5-C6 and C6-C7. Few studies investigated the effect of cervical disc degeneration on intervertebral motion patterns [25, 26, 40]. These studies limited their focus to flexion/extension ROM. In contrast to Simpson et al. [40], but similar to Miyazaki et al. [25] no significant correlation between intervertebral ROM and disc degeneration could be established in our study when each intervertebral level is investigated individually. However, when no distinction is made between the different intervertebral levels, i.e. all intervertebral levels are investigated as one group, a significant negative, but not very strong, correlation between ROM and intervertebral disc degeneration was observed for both flexion/extension and lateral bending. Every increase by 1 point in the degeneration score results in a ROM decrease of 0.5° in flexion/extension and 0.6° in lateral bending with respect to the average intervertebral ROM at a non-degenerated level. The same result yields for the correlation between disc degeneration and AP and lateral translation: a significant negative, but not very strong, correlation was observed for flexion/extension and lateral bending, when no distinction is made between the different intervertebral levels, i.e. all intervertebral levels are investigated as one group.
Our results can be useful for cervical arthroplasty because it remains unclear whether the goal of arthroplasty is to maintain or to restore motion at the operated level. In most of the radiological and clinical studies with arthroplasty,

the preoperative situation is used as a benchmark [36, 35, 30]. However, the maintenance of motion does not necessarily translate into the restoration of normal motion in the spine [31]. Our results could be used to bench mark postoperative continuous motion of patients operated with an intervertebral disc against motion data of healthy normal volunteers.

It must be emphasized that the aforementioned correlations between intervertebral ROM and disc degeneration are significant but not strong due to the large interindividual variation in ROM: intervertebral ROM of individuals with no degeneration (degeneration score=0) ranged from 0.2° to 25° for flexion/extension and from 0.3° to 19° for lateral bending. It must also be noted that both Simpson et al. and Miyazaki et al. investigated symptomatic patients, whereas this study examined asymptomatic healthy volunteers.

Our results show that ROM of a level adjacent to a severely degenerated level (degeneration score ≥ 7) is significantly higher than adjacent to a level free of degeneration (degeneration score = 0). Intervertebral ROM of such a level is 4.9% higher during flexion/extension, 1.4% during lateral bending and 1.3% during axial rotation on average. This indicates that the levels adjacent to a severely degenerated level will try to compensate the loss of motion due to intervertebral disc degeneration at that level, similar, however less pronounced, to the increase in ROM as sometimes seen adjacent to an interbody fusion [33, 37, 22].

5.5 Conclusion

Age has no predominant effect on the quantity or quality of motion during flexion/extension, lateral bending and axial rotation for individuals under 60. ROM and translation are significantly correlated during flexion/extension and lateral bending. Intervertebral disc degeneration increases according to age, especially at C5-C6 and C6-C7 which are operated upon most for intervertebral disc disease. A more degenerated spinal unit tends to have reduced mobility in asymptomatic individuals in particular during flexion/extension and lateral bending. Levels adjacent to a severely degenerated level partially compensate the loss of motion in all planes. This loss of motion is probably caused by intervertebral disc degeneration at that level.

Acknowledgments

Medtronic (TN, USA) is gratefully acknowledged for the institutional research and education grant. Jan Leemans and Guido Pauwels are gratefully

acknowledged for their technical contribution during imaging.

Author's involvement

All authors, Joris Walraevens, Philippe Demaerel, MD, PhD, Paul Suetens, PhD, Jos Vander Sloten, PhD, and Jan Goffin, MD, PhD, were substantially involved in this multidisciplinary research. All radiological data was collected by Joris Walraevens and Jan Goffin. Radiological imaging of the volunteers was coordinated by Philippe Demaerel. Paul Suetens was involved in the development of the motion analysis tool. The data analysis was performed by Joris Walraevens and was supervised by Jos Vander Sloten and Jan Goffin. This manuscript was written up by Joris Walraevens and was reviewed by all authors.

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Chapter 6

Longitudinal prospective long-term radiographic follow-up after treatment of single-level cervical disc disease with the Bryan Cervical Disc

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Adapted from a manuscript published in Neurosurgery 67(3): 679-687 (2010)

Abstract

Objective To prospectively assess the intermediate and long-term radiographic characteristics of disc replacement surgery with the Bryan Cervical Disc, and to correlate these results with clinical outcome.
Methods Range of motion was measured using a validated tool. Intervertebral disc degeneration was assessed using a quantitative scoring system. Heterotopic ossification was evaluated using a previously published scoring system. Device stability was investigated by measuring subsidence and anteroposterior migration. General clinical patient outcome was assessed using Odom's classification system.
Results 89 patients were initially included in this prospective long-term study. One patient was reoperated at the index level and four at an adjacent level: those patients were not further analyzed. The mobility at treated level was preserved in >85% of our cases. The insertion of the prosthesis did not lead to an increase in mobility at the adjacent levels. The degeneration score increased at both adjacent levels. Heterotopic ossification was present in 34-39% of the cases depending on the follow-up point. No cases of anteroposterior migration or of subsidence were found. More than 82% of all patients had a good to excellent clinical outcome on the long run.
Conclusions The device maintains preoperative motion at the index and adjacent levels, seems to protect against acceleration of adjacent level degeneration as seen after anterior cervical discectomy and fusion, and remains securely anchored in the adjacent bone mass on the long run. Heterotopic ossification was frequently seen. The vast majority of all patients had a good to excellent clinical outcome.

6.1 Introduction and objective

Over the past years, many short- and intermediate-term radiological and clinical studies on cervical arthroplasty with the Bryan Cervical Disc (Medtronic, TN, USA) have been published providing most of the times satisfactory results [5, 8, 12, 13, 17, 18, 38, 36, 40, 45, 46]. However, each time the duration of follow-up was limited to four years or less.
A longer-term, longitudinal radiographic analysis can provide further insight in the evolution of numerous radiological outcome measures such as mobility at the index level and adjacent levels, adjacent level disc degeneration, heterotopic ossification, and device stability. Moreover, these radiographic results may have an important impact on the function of the device and clinical outcome of the patient on the long run.

Previous radiographic studies have shown that the Bryan Cervical Disc remains mobile in a majority of cases during the first postoperative years [37, 30, 12]. It is hypothesized that this mobility protects against an accelerated degeneration at the adjacent levels, as seen after interbody fusion [14, 35]. However, data is lacking on how mobility at the index level and adjacent levels varies and how degeneration at the adjacent levels really evolves over time.
Both heterotopic ossification at the index level as device loosening can cause improper functioning of the device on the long run. The development of heterotopic ossification after surgery with the Bryan Cervical Disc and other cervical disc replacements has been reported [12, 2, 3, 22, 26] and consequently questions were raised whether ossification develops and/or increases over time and if ossification indeed influences the functionality of the device. Numerous studies have shown excellent stability of the Bryan Cervical Disc at intermediate follow-up [45, 37, 23, 43]. However, minor initial postoperative anteroposterior migration of prostheses has also been reported in a few cases [13, 31]. The assessment of longer-term device stability is therefore necessary.
A recent long-term clinical study has reported encouraging clinical results after surgery with the Bryan Cervical Disc for cervical degenerative disc disease [15]. However, whether preservation of motion at the index level and evolution of adjacent level disc degeneration had an impact on the clinical outcome remained unanswered.
The purpose of this prospective long-term follow-up study is to longitudinally assess the change in motion at the index level and adjacent levels in addition to the evolution of disc degeneration at the adjacent levels up to 8 years after disc replacement surgery. Moreover, the presence and change of heterotopic ossification at the index level together with its influence on mobility of the device is investigated. Additionally, anteroposterior migration and subsidence is assessed to provide answers towards long-term stability of the device. Finally, these radiographic results are correlated with clinical outcome.

6.2 Materials and methods

6.2.1 Study design

This study reports the interim analysis of a radiographic prospective long-term (i.e. up to eight years following surgery) study of a consecutive series of patients who were treated with the Bryan Cervical Disc at the University Hospital Leuven, Belgium. Some clinical data is provided too. The patient population is identical to the single level cases of the detailed clinical study by Goffin et al. [15] and arose from two groups. The first one was part of a clinical European multicenter trial, which examined one- and two-level implantations of the device with a follow-up of 2 years [13, 12]. Of this 146 single- and bi-level European cohort, 41 one-level patients were operated upon in the University Hospital Leuven and were enrolled in this long-term study. An additional 48 consecutive one-level patients, operated upon in the same hospital immediately after the termination of the inclusion of patients in the first European multicenter trail, were also enrolled. The last patient for this study was enrolled on October 18, 2002. Both parts of the study were executed according to protocols that were reviewed and approved by the local ethics committee.

All patients who received the Bryan device had a preoperative diagnosis of symptomatic cervical disc degeneration with or without spondylosis, causing radiculopathy and/or myelopathy. Postoperatively they were prospectively examined with 2 year time-intervals. This is an ongoing study of which this report describes its status of May 2009.

6.2.2 Measurements

Range of motion (ROM) at the index and adjacent levels was defined as the intervertebral sagittal rotation between full flexion and extension. ROMs were measured on dynamic lateral radiographs using a custom developed and validated motion analysis tool with a measurement error of 0.3° and 0.3 mm and excellent inter- and intra-rater agreement (ICC$>$0.75) (J Walraevens et al., unpublished data). A level was classified as mobile if the ROM of that level was larger than 2°.

Intervertebral disc degeneration was assessed using an objective and quantitative scoring system [42]. The overall degeneration score was calculated based on three variables: height loss, anterior osteophytes and endplate sclerosis (table 6.7). This overall score ranges from 0 (no degeneration) to 9 (severe degeneration).

Heterotopic ossification (HO) at the index level was evaluated using the scoring system of Mehren et al. [26] which was modified from McAfee et al. [25]. The scoring system ranges from grade 0 (no HO present) to grade 4 (complete fusion of the treated segment without movement in flexion/extension) (table 6.2).

Table 6.1: Scoring system of cervical disc degeneration based on neutral lateral radiographs [42].

1. Height loss†	0%	0 points
Middle disc height compared	≤25%	1 points
to normal middle disc height	>25% - ≤50%	2 points
at an adjacent level	>50% - ≤75%	3 points
	>75%	4 points
2. Anterior osteophytes	No osteophytes	0 points
with respect to the AP diameter	≤ 1/8 AP diameter	1 point
of the corresponding VB	> 1/8 - ≤ 1/4 AP diameter	2 points
	> 1/4 AP diameter	3 points
3. Endplate sclerosis	No sclerosis	0 points
	Detectable	1 point
	Definite	2 points
Overall degree of disc degeneration	0 points (no degeneration)	
= 1 + 2 + 3	1-3 points (mild degeneration)	
	4-6 points (moderate degeneration)	
	7-9 points (severe degeneration)	

Table 6.2: Scoring system for heterotopic ossification developed by Mehren et al. [26] which was modified from McAfee et al. [25].

Score	**Criteria**
Grade 0	No HO present Grade I HO is detectable in front of the vertebral body but not in the anatomic intradiscal space
Grade II	HO is growing into the disc space. Possible affection of the function of the prosthesis
Grade III	Bridging ossifications which still allow movement of the prosthesis
Grade IV	Complete fusion of the treated segment without movement in flexion/extension

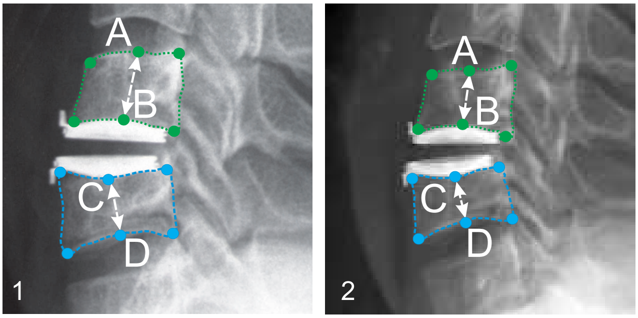

Figure 6.1: Subsidence is assessed on lateral radiographs and is defined as the sum of the change in vertebral body height comparing the immediate postoperative (1) and follow-up (2) situation. The height of the cranial and caudal vertebral body was defined by the length of AB and CD. A and C are located in the middle between the superior anterior and superior posterior corners of the cranial and caudal vertebral bodies. B and D located in the middle between the inferior anterior and inferior posterior corners of the cranial and caudal vertebral bodies.

Device stability was investigated by measuring the subsidence and anteroposterior migration of the device. Subsidence was assessed on lateral radiographs and was defined as the sum of the change in height of the cranial and caudal vertebral body between the immediate postoperative and follow-up situation (figure 6.1). A level was classified as subsided if the measured subsidence was larger than 2 mm [13]. Anteroposterior migration was determined on lateral radiographs and was defined as the sum of the cranial and caudal translation of the shells of the prosthesis with respect to the corresponding endplates between the immediate postoperative and follow-up situation (figure 6.2). A device was classified as migrated if the anteroposterior migration was larger than 3 mm [13].
Similar to the long-term clinical study on single- and double-level patients [15], general clinical patient outcome was assessed using Odom's classification [27] which categorizes the patient's outcome from 'excellent' to 'poor' and represents the degree of symptom relief and impairment improvement following surgery with respect to the preoperative status (table 6.3).

6.2.3 Statistical analysis

A P-value of 0.05 was considered significant. Linear correlations were investigated using the Spearman r correlation coefficient. A Student t-test

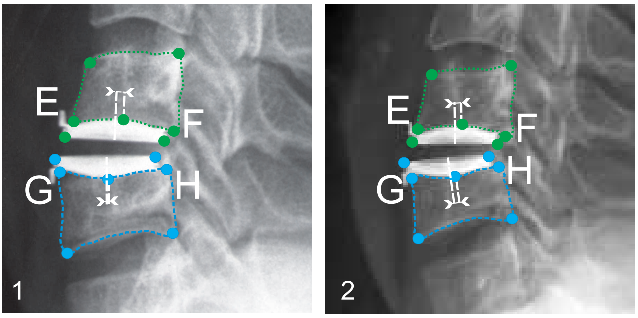

Figure 6.2: Anteroposterior migration is assessed on lateral radiographs and is defined as the sum of the cranial and caudal translation of the shells of the prosthesis with respect to the corresponding endplates of the vertebral bodies comparing the immediate postoperative (1) and follow-up (2) situation. The locations of the shells with respect to vertebral bodies at each follow-up point were defined as the distance between the middle point between EF and B for the cranial vertebra and the distance between the middle point between GH and C for the caudal vertebra. Translations were defined as the difference between the location of the prosthesis at immediate and longer follow-up along EF for the cranial vertebra and along GH for the caudal vertebra.

Table 6.3: Odom classification for general clinical outcome [27].

Score	**Criteria**
Excellent	All pre-operative symptoms relieved, able to carry out daily occupations without impairment
Good	Minimum persistence of pre-operative symptoms, able to carry out daily occupations without significant interference
Fair	Relief of some pre-operative symptoms, but whose physical activities were significant limited
Poor	Symptoms and signs unchanged or worse

was used to compare both groups if the data was Gaussian and continuous. In other situations, a Mann-Whitney U-test was used.

6.3 Results

6.3.1 Study enrollment and demographics

The total patient population consisted of 89 one-level patients. Demographic information for all patients is presented in table 6.4.

Table 6.4: Patient demographic information. SD: standard deviation

Characteristics	Total (n=89)
Age (yrs)	
Mean +/- SD (n)	42.8 +/- 8.0 (89)
Range	27.4 - 61.8
Weight (kg)	
Mean +/- SD (n)	74.8 +/- 18.5 (88)
Height (cm)	
Mean +/- SD (n)	170.0 +/- 10.0 (85)
Sex (n (%))	
Male	38 (42.7)
Female	51 (57.3)

In addition to the 89 cases who were initially included in the study, two more patients were already reoperated at the index level during the first two postoperative years, i.e. before the long-term study started. As a consequence these two patients did not participate in this long-term study [15]. In May 2009, all study-patients reached the 4 and 6 years follow-up time point. At 4 years follow-up, two of those study-patients were reoperated at an adjacent level [15]; these patients were consequently excluded from the study.

Between 4 and 6 years follow-up, three additional study-patients were excluded from the study: one patient was reoperated at the index level and two at an adjacent level [15].
So far, a total of 26 patients reached the 8 years follow-up point. One patient died due to none device related reasons between 6 and 8 years follow-up. Three out of the five study-patients who were excluded because of a reintervention, had their first operation earlier than May 2001: as a consequence those three patients would have reached 8 years follow-up in May 2009 if they would have stayed in the study.

The total number of patients who had a clinical and/or radiographic assessment at each follow-up point is indicated in table 6.5.

6.3.2 Radiographic outcome

Preoperatively, 89% of the patients had a mobile index level. At 4 years follow-up, 85% of the devices were mobile too. Seven out of 8 levels that were immobile preoperatively regained mobility at 4 years follow-up. Nine out of 67 preoperative mobile levels lost mobility. At 6 years follow-up 87% of the patients had mobile devices. At 8 years 88% of the patients who reached this follow-up point remained mobile. On average, preoperative ROM was 8.9+/-5.7° at index level. ROM stabilized around the preoperative value at 4 years (+6%), 6 years (+7%) and 8 years follow-up (-5%) ($P>0.05$; figure 6.3; table 6.6). Preoperative ROM of the index level was mildly but significantly correlated with postoperative ROM at 4 years, 6 years and 8 years follow-up ($r>0.36$, $P<0.05$).
At the cranial and caudal adjacent levels preoperative ROM was 11.1+/-5.0° and 9.5+/-5.4° on average. At follow-up, ROM stayed close to the preoperative value at 4 years (cranial +12%; caudal +11%), 6 years (cranial -4%; caudal +15%) and 8 years follow-up (cranial -4%; caudal +4%) ($P>0.05$; figure 6.3; table 6.6). Similar to the index level, preoperative ROM was significantly correlated with postoperative ROM at every follow-up time at the cranial ($r>0.51$; $P<0.05$) and caudal ($r>0.50$ $P<0.05$) adjacent level.

Table 6.5: Patient numbers for radiographic (flexion/extension) and clinical assessment at each follow-up point. And the number of patients that were lost to follow-up with respect to the preoperative situation, ‡including reoperation cases. †81 flexion/extension radiographs and 4 neutral radiographs. *81 flexion/extension radiographs and 1 neutral radiograph. ^{x}76 flexion/extension radiographs and 1 neutral radiograph. °26 flexion/extension radiographs. TBD: to be determined

	Radiographic assessment	**Clinical assessment**	**Lost to follow-up‡**
Preop	85†	/	/
4 yrs. follow-up	82*	82	7
6 yrs. follow-up	77^x	79	10
8 yrs. follow-up	26°	25	TBD

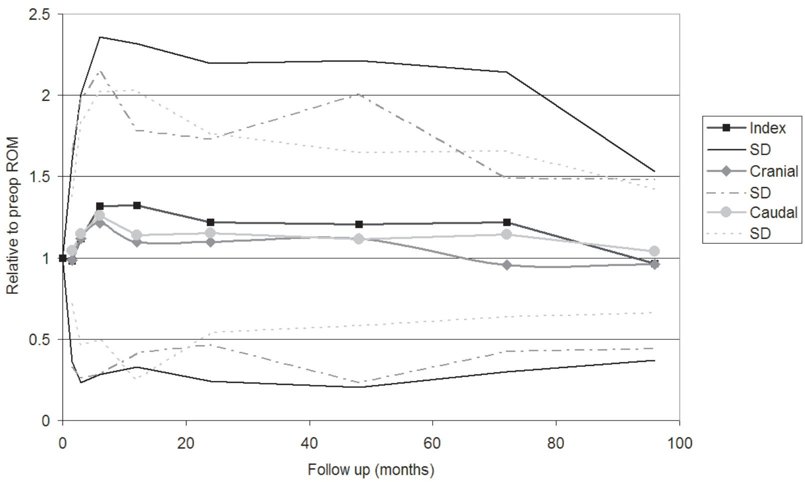

Figure 6.3: Mean relative intervertebral motion of the index and adjacent levels in function of follow-up time. Postoperative motion was calculated relative to the preoperative value.

Table 6.6: Range of motion (ROM) of the index and cranial and caudal adjacent levels in function of follow-up. Mean +/- standard deviation

	Nr	**ROM index (°)**	**ROM cranial (°)**	**ROM caudal (°)**
Preop	81	8.9+/-5.7	11.0+/-5.0	9.5+/-5.4
4 yrs. follow-up	81	7.9+/-5.7	11.0+/-4.7	9.7+/-4.7
6 yrs. follow-up	76	8.2+/-6.0	9.9+/-4.9	9.4+/-4.8
8 yrs. follow-up	26	8.0+/-5.1	10.0+/-5.5	12.2+/-4.6

On average, the preoperative intervertebral disc degeneration score was 2.4+/-2.0 at the index level. Preoperative disc degeneration was significantly negatively correlated with preoperative ROM at that level ($r=-0.27$; $P<0.05$). Preoperative intervertebral disc degeneration was 1.1+/-1.6 at the cranial and 0.7+/-1.3 at the caudal adjacent level (table 6.7). The degeneration score of the cranial adjacent level increased significantly at 4 years, 6 years and at 8 years follow-up (figure 6.4; $P<0.01$). For the caudal adjacent level this was true at 4 years and 6 years follow-up ($P<0.01$). There was a significant correlation between preoperative and postoperative degeneration for both adjacent levels at every follow-up time ($r>0.80$ and $r>0.67$, $P<0.05$).
At 4 years follow-up, 66% of the patients were HO free (grade 0), 5% had grade 4 HO causing immobility of the device (table 6.8). At 6 years follow-up, 62% of

Table 6.7: Overall degree of disc degeneration at the cranial and caudal adjacent levels in function of follow-up. The degeneration score (0-9) was determined based on an objective scoring system [42]. Mean +/- standard deviation. *significant different compared to the preoperative situation (P<0.05).

	Nr	**Degeneration cranial (0-9)**	**Degeneration caudal (0-9)**
Preop	85	1.1+/-1.6	0.7+/-1.3
4 yrs. follow-up	82	1.6+/-1.8*	1.4+/-1.7*
6 yrs. follow-up	77	1.8+/-1.9*	1.4+/-1.8*
8 yrs. follow-up	26	2.3+/-2.1*	1.0+/-1.6

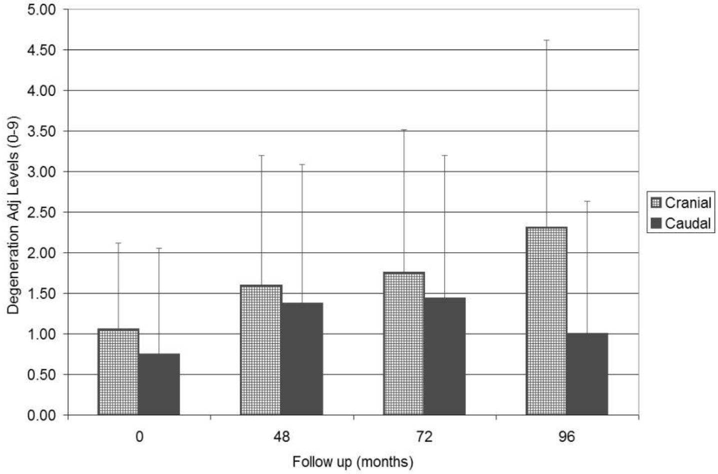

Figure 6.4: Evolution of mean adjacent level disc degeneration in function of follow-up time, based on an objective scoring system ranging from 0 (no degeneration) to 9 (severe degeneration) [42].

the patients were HO free, 8% had grade 4 HO. At 8 years follow-up, 61% of the patients were HO free, 8% had grade 4 HO. There was no significant increase in HO when comparing 4 years follow-up to 6 and 8 years follow-up (P>0.05). No correlation between postoperative HO and preoperative ROM nor degeneration at the index level was observed (P>0.05). At 4 and 6 years follow-up, there was a mild but significant negative correlation between postoperative HO and ROM at the same follow-up point (r<-0.24, P<0.05).

Table 6.8: Occurrence of heterotopic ossification (HO) in function of follow-up, based on the scoring system of Mehren et al. [26]

	n	**No HO** (Grade 0)	**Mobile HO** (Grades 1-3)	**Immobile HO** (Grade 4)
4 yrs. follow-up	82	54 (66%)	24 (29%)	4 (5%)
6 yrs. follow-up	77	48 (62%)	23 (30%)	6 (8%)
8 yrs. follow-up	26	16 (61%)	8 (31%)	2 (8%)

At all follow-up points, no cases of anteroposterior migration greater than 3 mm or subsidence above 2 mm were observed. The mean amount of migration was 0.83+/-0.58 mm at 4 years, 0.88+/-0.61 mm at 6 years and 0.97+/-0.85 mm at 8 years follow-up (table 6.9). There was no significant increase between the different time points (P>0.05). The mean amount of subsidence was 0.69+/-0.45 mm at 4 years, 0.72+/-0.59 mm at 6 years and 0.77+/-0.69 mm at 8 years follow-up (table 6.9). There was no significant increase between the different time points (P>0.05).

6.3.3 Clinical outcome

It first needs to be rementioned that two patients were already reoperated at the index level during the first two postoperative years, i.e. before the long-term

Table 6.9: Anteroposterior migration and subsidence in function of follow-up. Mean +/- standard deviation.

	n	**AP migration (mm)**	**Subsidence (mm)**
4 yrs. follow-up	82	0.83+/-0.58	0.69+/-0.45
6 yrs. follow-up	77	0.88+/-0.61	0.72+/-0.59
8 yrs. follow-up	26	0.97+/-0.85	0.77+/-0.69

Table 6.10: Clinical outcome of all study-patients in function of time expressed using the Odom scores [27]. Study-patients who were operated earlier than May 2001 and consequently would have reached the 4, 6, and 8 years follow-up point if they would have stayed in the study, are considered as poor clinical outcomes.

	n	Excellent	Good	Fair	Poor
4 yrs. follow-up	84	49 (58%)	24 (29%)	8 (10%)	3 (3%) (including reoperations: n=2)
6 yrs. follow-up	84	40 (48%)	31 (37%)	7 (8%)	6 (7%) (including reoperations: n=5)
8 yrs. follow-up	28	17 (61%)	6 (21%)	2 (7%)	3 (11%) (including reoperations: n=3)

follow-up study started: they did not participate in this long-term follow-up study. At 4 years follow-up, two study-patients were reoperated at an adjacent level. Between 4 and 6 years follow-up, one study-patient was reoperated at the index level and two at an adjacent level [15].
If the study-patients who were reoperated upon are considered to have a poor outcome, 87% had a good to excellent clinical outcome at 4 years follow-up; 10% scored fair; and 3% was doing poorly at that same time point. At 6 and 8 years follow-up, 85% and 82% had a good to excellent clinical outcome; 7% and 11% was doing poorly (table 6.10).
Clinical outcome was mildly but significantly correlated with motion at the index level at 4 and 6 years follow-up ($r=0.34$ and $r=0.29$; $P<0.05$). At 8 years follow-up this relation was not significant. No significant correlation between clinical outcome and the maximum of cranial and caudal adjacent level disc degeneration was found at 4, 6 and 8 years follow-up ($P>0.05$). At 6 and 8 years follow-up, clinical outcome was significantly and negatively correlated with the maximum progression in degeneration score of the cranial or caudal adjacent level compared to the preoperative situation ($r=-0.31$ and $r=-0.59$; $P<0.05$). No significant correlation between clinical outcome and postoperative heterotopic ossification, anteroposterior migration or subsidence at the index level at every follow-up point could be established ($P>0.1$).

6.4 Discussion

We performed a prospective, longitudinal radiographic study assessing the change in motion at the index level and adjacent levels in addition to the evolution of adjacent level disc degeneration up to 8 years after disc replacement surgery with the Bryan Cervical Disc. Moreover, we investigated the presence and change of heterotopic ossification at the index level and its influence on the function of the device. Next, the device stability was evaluated by measuring anteroposterior migration and subsidence of the device in the adjacent bone mass. Finally, to put these radiological results into perspective, the results were correlated with clinical outcome.

In literature, data is lacking on how mobility of the Bryan Cervical Disc and of the adjacent levels evolves over time on the long run. Our results indicate that motion is maintained at the index level up to 8 years after surgery for most of the patients (e.g. figure 6.5). However, it would be erroneous to claim that motion is restored to normal. The range of motion was significantly lower than normal values for C5-C6 and C6-C7 which range typically from 10° to 20° [35, 11, 29, 34]. A strong correlation between preoperative and postoperative ROM of the index level suggests that a preoperative mobile level will have a higher chance of remaining mobile on the long run. Nevertheless we were surprised to observe that a high number of preoperatively immobile index levels regained and maintained mobility after insertion of the prosthesis. The threshold of 2° was chosen analogous to previous clinical studies [13, 12, 15] to enable comparison. The error for measuring intervertebral rotation is considerably lower than this threshold and has therefore a negligible influence on the results.

Short term studies showed only a nonsignificant increase in adjacent segment motion after insertion of the Bryan Cervical Disc of less than 10% at 2 years after surgery [37, 20, 32]. Our results confirm these findings on the long run. It appears that the prosthesis protects against an increase in adjacent level motion as sometimes seen after interbody fusion [4, 6, 7, 24, 33, 39, 44].

Probably the most important goal of artificial disc surgery of the cervical spine is to prevent acceleration of adjacent level degeneration, as often seen after interbody fusion [19, 14, 35]. A prosthesis will off course not prevent the progression of natural age-related disc degeneration. Gore et al. performed a ten-years follow-up study on asymptomatic healthy subjects. They found that 34% of subjects without initial cervical disc degeneration developed degenerative radiographic features at 10 years and that 79% of subjects with evidence of initial degeneration had evidence of progression at 10 years [16]. Similarly, in our study 37% and 32% of the patients without any initial degeneration at the cranial and caudal adjacent levels developed degenerative radiographic features at those levels at 6 years and 8 years follow-up respectively. In patients with or without evidence of initial degeneration at the adjacent levels, 48% and 44% had evidence of progression at the cranial and/or caudal adjacent level at 6 years and 8 years (figure 6.6). Goffin et al. performed a long-term follow-up study with a mean follow-up of 8 years (5-15y) on 180 patients who were treated with anterior cervical discectomy and fusion. They found that after fusion, 92% of patients had additional degeneration

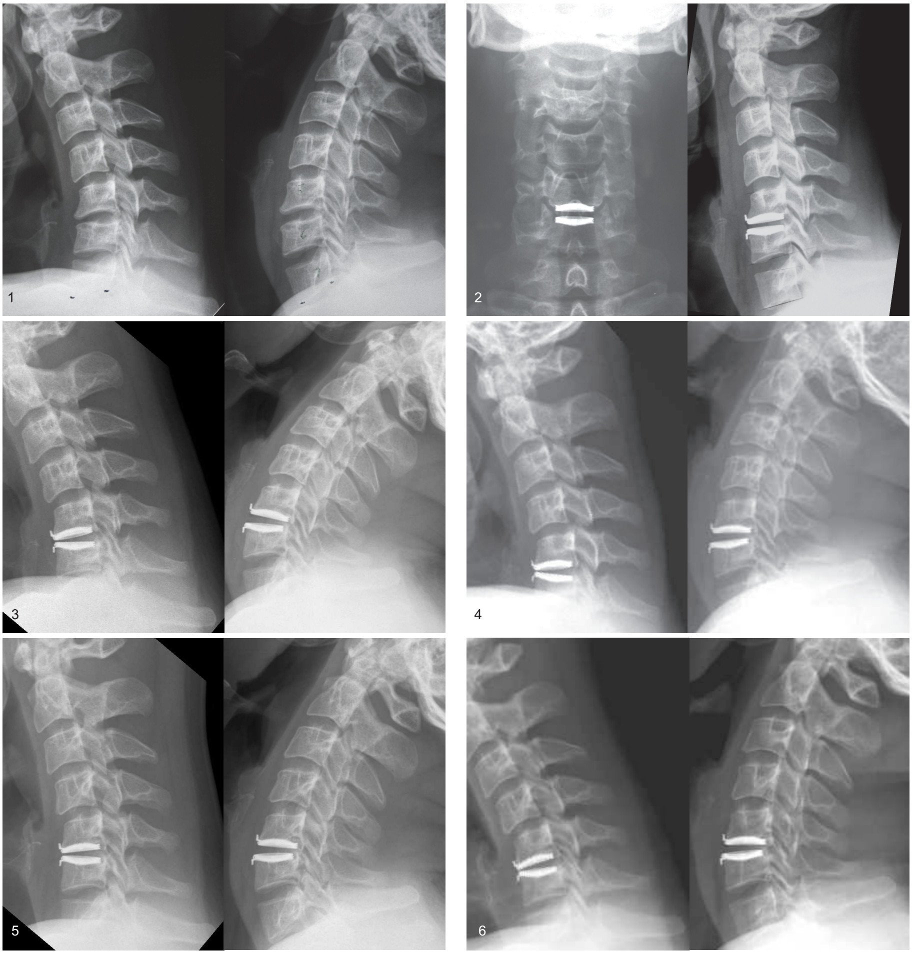

Figure 6.5: Preoperative (1) flexion and extension lateral radiographs, immediate postoperative (2) neutral frontal and lateral radiographs, as well as 2 years (3), 4 years (4), 6 years (5), and 8 years (6) postoperative flexion and extension lateral radiographs.

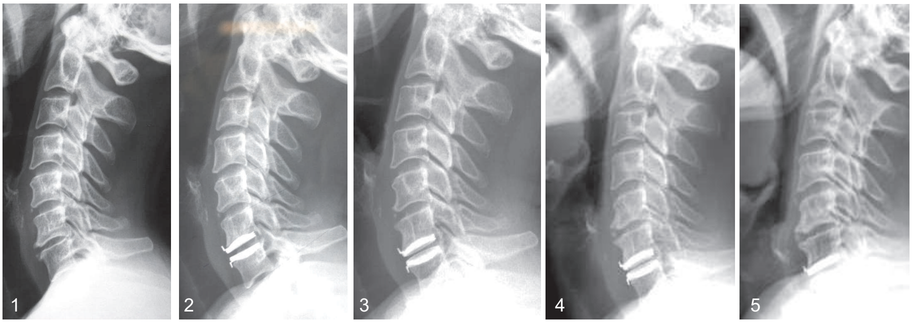

Figure 6.6: A preoperative (1), 2 years (2), 4 years (3), 6 years (4) and 8 years (5) postoperative plain radiograph of a patient who had progression of adjacent level disc degeneration at C5-C6 after insertion of a Bryan Cervical Disc at C6-C7.

at the cranial and/or caudal adjacent disc levels at in comparison with the initial radiographic findings [14]. This yielded not only for older non-trauma cases but also for younger trauma cases without preexisting degenerative disc disease. Similar to the results of Robertson et al. [35], our results suggest that disc replacement surgery seems to protect against acceleration of degeneration at the adjacent levels, as often seen after interbody fusion. However, it needs to be mentioned that in total four patients needed a reoperation at an adjacent level.

The development of heterotopic ossification and the stability of the device can have an important influence on the long-term function of the device. Heterotopic ossification has been previously reported after cervical arthroplasty with a Bryan Cervical Disc [2, 22, 28, 12] and other cervical devices [3, 26]. At 1 year follow-up Leung et al. reported that 17.8% of a 90-patient Bryan group showed incidence of HO. A total of 4.4% of the patients were immobile [22]. At the same follow-up point, Mehren et al. found an incidence of HO 66.2% after surgery with the ProDisc-C; 9.1% of the patients were immobile [26]. At 8 years follow-up, our results lay within these previously reported values. In total, 39% of the patients show evidence of HO on plain lateral radiographs; 8% is immobilized at the index level at that follow-up point. However, the increase in HO was minimal and not significant when comparing 4 years to 8 years follow-up (figure 6.7). Besides, 94% of the patients who were HO free at 4 years after surgery remained HO free up to 8 years postoperative. Unsurprisingly, our results show that HO has an important influence on the postoperative motion of the device. So to ensure long-term proper function of the prostheses, HO should be minimized. It has been mentioned that prophylactic use of non-steroidal anti-inflammatory drugs (NSAIDs) for the duration of 2 weeks from

Figure 6.7: A preoperative (1), 2 years (2), 4 years (3), 6 years (4) and 8 years (5) postoperative plain radiograph of a patient who developed heterotopic ossification at the index level at 2 years postoperative (Grade 3). Nevertheless the bridging ossification, motion at the index level was maintained (>2°) at 2 years (6) up to 8 years after surgery (7).

the moment of surgery, might prevent development of HO [9, 1, 10, 41]. NSAIDs were not routinely used in our long term follow-up study. Less than 10% of the patients received NSAIDs for 3-4 days for treating initial postoperative residual neck or arm pain.

Besides the development of heterotopic ossification at the index level, an unstable fixation of the device in the adjacent bone mass might also result in improper functioning of the prosthesis. A prospective and highly accurate radiostereometric study of 11 single-level patients operated with a Bryan Cervical Disc showed immediate and continued stability of the device up to 2 years after surgery [23]. These results were confirmed by others [21, 43, 45, 37]. However, some cases of device instability have been observed. Goffin et al. reported evidence of discrete initial postoperative anterior migration of one device and suspected it in a second patient in their 2 years follow-up study [12, 13]. Similarly, Pickett et al. found a case of delayed migration in one patient with postoperative segmental kyphosis out of 74 patients operated with a Bryan Cervical Disc [30]. Our results prove that the device is securely anchored in the vertebral bodies and remains fixed up to 8 years after surgery. No cases of anteroposterior migration more than 3 mm or subsidence more than 2 mm were observed. The 2 cases that were mentioned in the initial study [12, 13] were early cases in which insufficient milling of the concavities in the adjacent vertebral bodies for receiving the shells of the prosthesis might have been the reason for the migration. There was no further migration of those prostheses anymore on the long run. At 4, 6 and 8 years after surgery, the quantity of migration for both patients was lower than the postulated threshold of 3 mm.

The aforementioned radiographic results are interesting and meaningful from a biomechanical and radiological point of view. However, the final purpose of new technologies such as cervical total disc prostheses should be to improve patient clinical outcome on the long run in comparison to what is achieved with interbody fusion. Therefore, the radiographic results were correlated with general clinical outcome. In total, three of our patients needed a reoperation at the index level: two of these three patients did not participate in this long-term follow-up study since these reinterventions were already performed during the first two postoperative years in another institution [15]. The third intervention was performed in our department at 6 years after surgery [15]. These three reoperations at the index level may be considered as adverse events. Four patients needed a second operation at an adjacent level [15]. More than 82% of all study-patients had a good to excellent clinical outcome, in terms of Odom scores; this satisfying clinical result was maintained up to 8 years postoperatively. This is comparable to other recent clinical studies [18, 36, 15]. Moreover, our results show that patients who have a postoperative mobile index level tend to have a better clinical outcome. Nevertheless, as the correlation is significant but not strong, other factor, such as age, gender, and body weight might also have an impact on postoperative mobility of the index level. Additionally, patients who only had a small progression in disc degeneration at the adjacent levels are inclined to have better clinical outcome compared to those with a more pronounced increase of disc degeneration at those levels. Heterotopic ossification, anteroposterior migration and subsidence seemed not to influence clinical outcome. However, to ensure proper long-term functionality of the device, these possible complications can not be neglected and should be carefully followed-up.

6.5 Conclusion

Mobility of treated level is maintained up to 8 years after surgery in a vast majority of our cases. Moreover, the insertion of the prosthesis did not lead to an increase in mobility of the adjacent levels and seems to protect against

acceleration of adjacent level degeneration, as often seen after interbody fusion. Heterotopic ossification was present in approximately 40% of all patients at all follow-up points; 8% of the patients were immobilized due to the ossification. Heterotopic ossification did not seem to have progressed at 8 years compared to 4 years follow-up.
No cases of anteroposterior migration or of subsidence were found. The prosthesis appears to be securely anchored in the adjacent bone mass and remains stable up to 8 years after surgery.
More than 82% of all patients had a good to excellent clinical outcome on the long run. A mobile prosthesis and little progression in degeneration at the adjacent levels appear to promote better clinical outcome.

Acknowledgments

Medtronic (TN, USA) is gratefully acknowledged for the institutional research and education grant.

Author's involvement

All authors, Joris Walraevens, Philippe Demaerel, MD, PhD, Paul Suetens, PhD, Frank Van Calenbergh, MD, Johan van Loon, MD, PhD, Jos Vander Sloten, PhD, and Jan Goffin, MD, PhD, were substantially involved in this multidisciplinary research. Radiological imaging of the patients was coordinated by Philippe Demaerel. All clinical and radiological data was collected by Joris Walraevens and Jan Goffin. Paul Suetens was involved in the development of the motion analysis tool. The data analysis was performed by Joris Walraevens and was supervised by Jos Vander Sloten and Jan Goffin. Disc replacement surgeries were performed by Jan Goffin, Johan van Loon, and Frank Van Calenbergh. This manuscript was written up by Joris Walraevens and Jan Goffin and was reviewed by all authors. This research was coordinated by Jan Goffin.

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Chapter 7

Radioscopic comparison of cervical motion patterns of patients operated with a Bryan Cervical Disc versus healthy volunteers

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To be submitted for publication in Spine

Abstract

Introduction Cervical disc prostheses are designed to permit normal motion. The scope of this study was to compare quantitative and qualitative motion patterns of patients operated with a Bryan Cervical Disc Prosthesis (Medtronic, Memphis, USA) with a control group of healthy volunteers.

Methods Continuous flexion/extension motion patterns of 10 patients who were operated for cervical disc disease with a Bryan Cervical Disc Prosthesis inserted at C5-C6 (Bryan group) were compared with 15 asymptomatic age-matched volunteers (healthy control group). Motion patterns were assessed using preoperative flexion and extension radiographs together with fluoroscopic images at 1 and 6 years after surgery for the Bryan group and using fluoroscopic images for the healthy control group. Quantitative motion patterns, i.e. range of motion (ROM) and anteroposterior (AP) translation, as well as continuous, qualitative parameters such as continuous angular motion (CAM), continuous AP translational motion (CTM) and center of rotation (COR) were calculated using a custom development motion analysis tool.

Results There was no significant difference in age between both groups ($p>0.1$). No significant difference in ROM was observed between the Bryan group preoperatively, 1 and 6 year postoperatively and the healthy control group ($p>0.05$). AP translation in the Bryan group was, preoperatively as well as at 1 and 6 years postoperatively, significantly smaller than in the healthy group ($p<0.05$). However, within the Bryan group no significant difference in preoperative versus 1 and 6 years postoperative AP translation was seen ($p>0.05$). Moreover, there was no significant difference in the location of the center of rotation between the Bryan group pre- and 1 and 6 year postoperatively and the healthy control group ($p>0.05$). CAM during flexion/extension showed a similar trend in both groups and did not significantly differ between the healthy group and the Bryan group 1 and 6 year postoperatively. Although the trend for CTM was similar for both groups, it was significantly smaller in the Bryan group at 1 and 6 year after surgery ($p<0.05$) compared to the healthy control group.

Conclusions The Bryan prosthesis is able to mimic normal intervertebral ROM, continuous angular motion and a physiological center of rotation. This does not yield for AP translation and continuous translational motion. Nevertheless, both the quantity as quality of AP translation was maintained with respect to the preoperative situation after insertion of the prosthesis.

7.1 Introduction and objective

One of the goals of cervical arthroplasty is to maintain motion after anterior cervical discectomy. The rationale behind this is to prevent acceleration of disc degeneration as seen at levels adjacent to an interbody fusion [2, 18].
Many radiographic and clinical studies have demonstrated that intervertebral disc prostheses are able to maintain motion up to short, intermediate and longer follow-up. However, most of these studies were limited to the assessment of intervertebral range of motion (ROM) [3, 7, 9, 13, 14, 26, 30, 33, 34]. Few studies investigated anteroposterior (AP) translation and the location of the center of rotation (COR) after disc replacement surgery [25, 24, 19, 20]. In most of these studies, the preoperative situation was used as a benchmark. However, the maintenance of motion does not necessarily translate into the restoration of normal motion in the spine [20]. Only Goffin et al. [11], and Rousseau et al. [23] used a control group of normal individuals to compare intervertebral motion patterns of disc replaced patients. Goffin et al. measured intersegmental motion using fluoroscopic images during flexion/extension of 10 normal healthy volunteers and of 10 patients with a C5-C6 disc replacement. They found that disc replacement patients had a comparable range of motion and continuous angular motion during flexion/extension as normal volunteers [11]. Rousseau et al. compared intervertebral kinematics after a ball-and-socket total disc arthroplasty using full flexion/extension radiographs and observed that neither a cranial nor a caudal type of ball- and-socket design did fully restore the normal mobility in terms of ROM and COR in their series [23].
None of the aforementioned studies investigated the combination of continuous motion patterns and the location of the COR of disc replaced subjects and compared it with a healthy control group. The scope of this study was therefore to compare quantitative and qualitative motion patterns of patients operated with a Bryan Cervical Disc Prosthesis with those of healthy volunteers.

7.2 Materials and methods

7.2.1 Study design and set-up

This study compares the lateral kinematics of the cervical spine of two groups: patients who were treated with the Bryan Cervical Disc (Bryan group) and healthy volunteers as control (healthy control group).
The Bryan cohort consists of a consecutive series of 10 patients who were treated at the C5-C6 level with the Bryan Cervical Disc at the University Hospital Leuven, Belgium, between 2001 and 2002. They had full flexion and

extension radiographs preoperatively and had a lateral fluoroscopic assessment at 1 year and 6 years after surgery. The Bryan group is part of the patient population described by in the detailed clinical study by Goffin et al. [12] and the radiological study by Walraevens et al. [30]. Moreover, this cohort is part of a clinical European multicenter trial, which examined one- and two-level implantations of the device with a follow-up of 2 years [10, 9]. The patients who received the Bryan device had a preoperative diagnosis of symptomatic cervical disc degeneration with or without spondylosis, causing radiculopathy and/or myelopathy at C5-C6.
The healthy control group is part of a larger study group of 60 volunteers equally divided over 4 age groups: group I (18-30 years), group II (31-40 years), group III (41-50 years) and group IV (51-60 years) (Walraevens et al., unpublished data). For this study, the fluoroscopic image sequences of group III, which consists of 15 healthy asymptomatic individuals, were analyzed. Volunteers with a history of neck pain, previous neck trauma or neck surgery, and pregnant or breastfeeding women were excluded from this study.
Before the movement was recorded, the patients and volunteers were coached to maximally flex and extend their neck and to prevent out-of-plane movement. Each movement was performed within a 6 to 8-second period. A led skirt was provided to protect the lower body. During measurement the patient or volunteer sat in an upright position, knees flexed at 90°. This study obtained approval from the Radioprotection Department and the Ethics Committee (UZ Gasthuisberg, Leuven, Belgium). All volunteers signed an informed consent.

7.2.2 Measurements

Intervertebral disc degeneration was assessed using a validated, objective and quantitative scoring system [29]. On lateral radiographs, the overall degeneration score is calculated based on three variables: height loss, anterior osteophytes and endplate sclerosis. Each variable contributes with decreasing importance to the total degeneration score. The overall score ranges from 0 (no degeneration) to 9 (severe degeneration). For the Bryan group, disc degeneration was measured at the preoperative time point.
Motion patterns were assessed based on a lateral image sequence during flexion/extension and were calculated using a custom developed semi-automatic motion analysis tool (e.g. figure 7.1). This tool has an excellent repeatability (intraclass correlation coefficient [28]>0.77) and a low measurement error [5] (0.3° and 0.4 mm) (Walraevens et al., unpublished data). Continuous angular motion (CAM) (figure 7.2) as well as continuous AP translational motion (CTM) (figure 7.3) and the location of the COR, based on full flexion and extension, were calculated. AP translation was defined as the translation

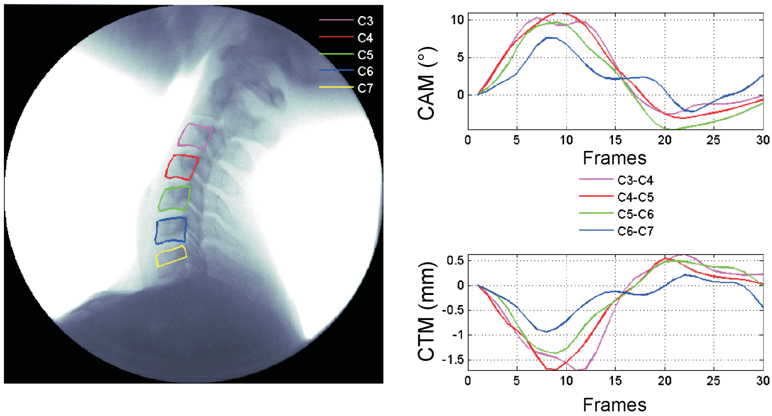

Figure 7.1: Continuous angular motion (CAM), continuous anteroposterior translational motion (CTM) during flexion/extension. Frame 0: neutral position, frame 9: full flexion position, frame 21: full extension position, frame 30: neutral position.

of the geometric center of the cranial vertebral body along an axis parallel to the cranial endplate or shell of the prosthesis of the caudal vertebral body. Translation was normalized to the width of the vertebral body [8]. Range of motion (ROM) was defined as the difference between maximal CAM during full flexion and minimal angular motion during full extension for each intervertebral level (figure 7.2). Similar, AP translation was defined as the difference between the maximal and minimal CTM during full flexion and extension for each intervertebral level (figure 7.3). These differences reflect the amount of intervertebral motion.
As the patients and volunteers flexed their necks at different speeds, the real number of frames of the fluoroscopic image sequence during flexion/extension was resampled and normalized to a virtual number, i.e. 30, to enable comparison. All assessments were done for intervertebral levels C4-C5 and C5-C6. In this study, level C6-C7 was not analyzed as this level was frequently not clearly visible in the lateral fluoroscopic image sequences due to the bony overlap of the shoulders with the lower cervical vertebrae.
Before the identification and tracking of the anatomical landmarks, geometric distortion caused by the image intensifier was minimized using a correction matrix. To obtain this matrix, an X-ray image of a calibration grid was taken for both fluoroscopic cameras. From this image, based on the prior knowledge of the grid, the correction matrix was calculated by mapping the original pixel coordinates to the corrected pixel.

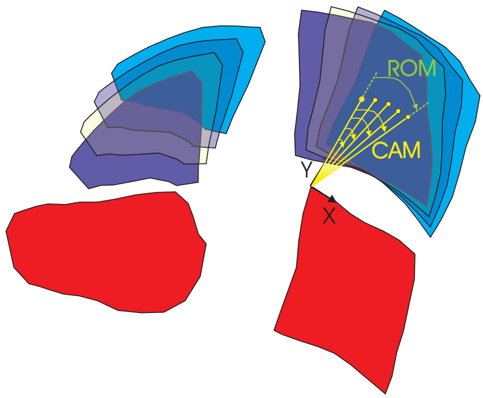

Figure 7.2: Calculation of continuous angular motion (CAM) and range of motion (ROM) during flexion/extension. ROM is defined as the difference between maximal CAM during full flexion and minimal CAM during full extension for each intervertebral level.

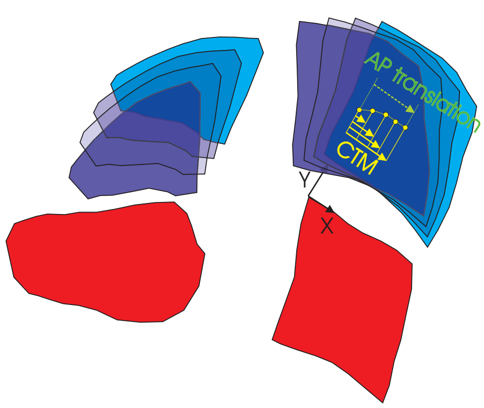

Figure 7.3: Calculation of continuous anteroposterior (AP) translational motion (CTM) and AP translation during flexion/extension. AP translation is defined as the translation of the geometric center of the cranial vertebral body along an axis parallel to the cranial endplate or shell of the prosthesis of the caudal vertebral body. AP translation is defined as the difference between maximal CTM during full flexion and minimal CTM during full extension for each intervertebral level.

Table 7.1: Summary of the demographics of the Bryan and healthy control group. Mean +/- standard deviation. *Measured at the preoperative situation.

	Bryan group	Healthy group	
Number	10	15	
Female / Male (Age (y)	48.2 +/- 6.6	45.4 +/- 3.1 (41-50)	p>0.05
Degeneration score (0-9)			
C4-C5	0.73+/-0.82*	0.40+/-0.51	p>0.05
C5-C6	1.70+/-1.64*	1.47+/-1.69	p>0.05

7.2.3 Statistical analysis

A p-value of 0.05 was considered significant. Linear correlations were investigated using the Spearman r correlation coefficient. A Student t-test was used to compare both groups if the data was Gaussian and continuous. In other situations, a Mann-Whitney U-test was used. The coefficient of multiple determination [15] was used to compare continuous motion curves.

7.3 Results

7.3.1 Demographics

Table 7.1 provides a summary of the demographic data of the Bryan and healthy control group. There is no significant difference in age between both groups ($p>0.05$). In total, 60% of the Bryan group is female compared to 73% of the healthy group.

7.3.2 Measurements

No significant difference in degeneration score is seen at C4-C5 as well as at C5-C6 between the Bryan group at the preoperative situation and the healthy control group (table 7.1; $p>0.05$).
When preoperative ROM and AP translation of the Bryan group is compared to the ROM at 1 and 6 years after surgery, no significant differences are found for C4-C5 and index level C5-C6 (table 7.2; $p>0.05$). Similarly, if CAM and CTM are compared within the Bryan group, no significant differences are observed when comparing the different follow-up points (figure 7.4 and 7.5; $p>0.05$). The coefficients of multiple determination between the 1 and 6 year

Table 7.2: Intervertebral range of motion (ROM) and anteroposterior (AP) translation during flexion/extension for the Bryan and healthy control group. AP translation was normalized to the width of the vertebral body. Mean +/- standard deviation.

		Bryan group	Healthy group	p
ROM				
C4-C5 (°)	preop	14.6+/-2.5	15.2+/-5.4	p>0.05
	1y postop	14.5+/-2.3		p>0.05
	6y postop	14.2+/-2.1		p>0.05
C5-C6 (°)	preop	13.2+/-6.6	15.7+/-3.5	p>0.05
	1y postop	12.5+/-4.7		p>0.05
	6y postop	13.0+/-3.5		p>0.05
AP translation				
C4-C5 (/)	preop	0.25+/-0.06	0.30+/-0.07	p<0.05
	1y postop	0.17+/-0.07		p<0.05
	6y postop	0.21+/-0.07		p<0.05
C5-C6 (/)	preop	0.16+/-0.07	0.25+/-0.09	p<0.05
	1y postop	0.13+/-0.06		p<0.05
	6y postop	0.14+/-0.05		p<0.05

postoperative situation are 0.96 at C4-C5 and 0.93 at C5-C6 for CAM and 0.95 at C4-C5 and 0.94 at C5-C6 for CTM. The preoperative location of the center of rotation does not differ from the 1 and 6 years postoperative position for both intervertebral levels (figure 7.6; $p>0.05$). When the preoperative, 1 year and 6 years postoperative ROM of the Bryan group is compared to the ROM of the healthy control group, no significant differences are found for both intervertebral levels (tabel 7.2; $p>0.05$). Similarly, if CAM of the healthy control group is compared to the Bryan group, no significant differences are observed at both time points for C4-C5 and C5-C6 (figure 7.4; $p>0.05$). The coefficients of multiple determination between the healthy control group and the 1 and 6 year postoperative situation of the Bryan group are 0.97 and 0.93 for C4-C5 and 0.92 and 0.95 for C5-C6. However, the preoperative, 1 year and 6 year postoperative AP translation of the Bryan group is significantly smaller than the AP translation of the healthy control group for both intervertebral levels (tabel 7.2; $p<0.05$).
In the same way, if the CTM of the healthy control group is compared with the Bryan group, significant differences are observed for C4-C5 and C5-C6 (figure 7.5; $p<0.05$). The coefficients of multiple determination between the healthy group and the 1 and 6 year postoperative situation are lower than for CAM: 0.71 and 0.87 for C4-C5 and 0.77 and 0.80 for C5-C6. The location of the

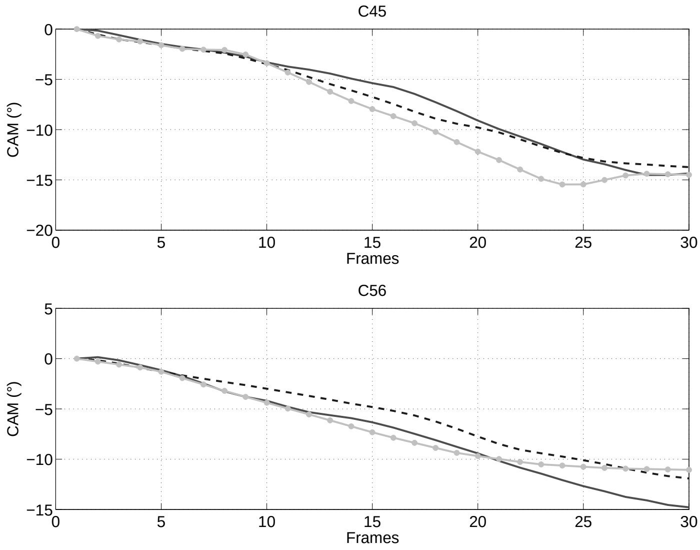

Figure 7.4: Continuous angular motion (CAM) during flexion/extension for the Bryan group (1 and 6 years postoperatively) and the healthy control group for levels C4-C5 and C5-C6 (index level). Frame 0: full flexion, frame 30: full extension.

center of rotation of the healthy group does not differ from the preoperative, and 1 and 6 year postoperative position at C4-C5 and C5-C6 of the Bryan group (figure 7.6; $p>0.05$).

7.4 Discussion

Cervical disc prostheses are designed to permit normal motion. Therefore the purpose of this study was to investigate quantitative motion patterns, e.g. intervertebral ROM and AP translation, and qualitative motion patterns, e.g. continuous angular motion, AP translation and the location of the center of rotation, of patients operated with a Bryan Cervical Disc Prosthesis and to compare them with a healthy control group using fluoroscopy.
As cervical motion patterns can be influenced by a lot of external factors, e.g. ROM measured from flexion to extension versus from extension to flexion, lack of effort, discomfort [6, 19], the tools to measure these motion patterns should be reliable and accurate. The semi-automatic motion tool used to

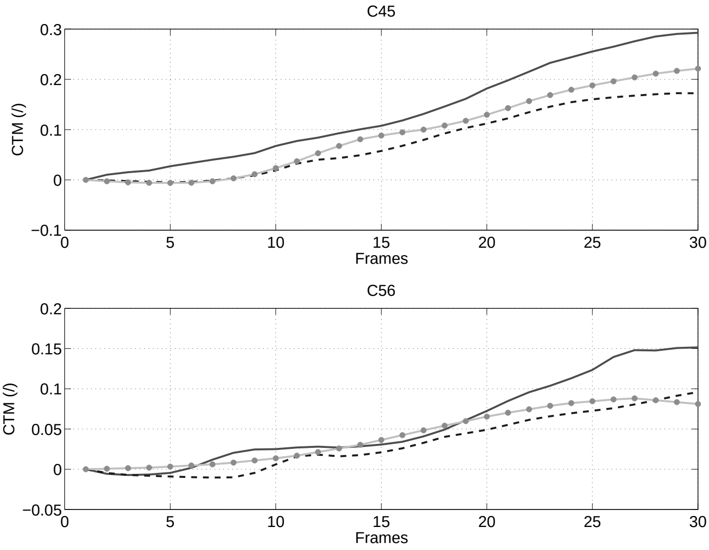

Figure 7.5: Continuous AP translational motion (CTM) during flexion/extension for the Bryan group (1 and 6 years postoperatively) and the healthy control group for levels C4-C5 and C5-C6 (index level). AP translation was normalized to the width of the vertebral body. Frame 0: full flexion, frame 30: full extension.

calculate intervertebral motion patterns is based on a generic model-based segmentation algorithm developed at Medical Image Computing (Radiology-ESAT/PSI, KULeuven, Belgium) [27]. It has an excellent repeatability (intraclass correlation coefficient [28]>0.77) and a low measurement error [5] (0.3°) (Walraevens et al., unpublished data). The accuracy is comparable to that of the QMA software by Medical Metrics Inc. (USA) which has proven its value in numerous studies [14, 25, 24, 21, 22].
First, to investigate whether the prosthesis was able to maintain motion, motion patterns of the Bryan cohort at 1 and 6 years after surgery was compared with the preoperative situation. Similar to previously found results our results suggests that the quantity of motion, i.e. ROM as well as AP translation, is maintained up to 6 years after surgery both at the index and at the cranial adjacent level [30, 12]. Moreover, our results indicate that also the quality of motion, characterized by CAM, CTM and the location of the COR, remains unchanged with respect to the preoperative situation. This is equally important because with the location of the COR preserved, the facets and ligaments are

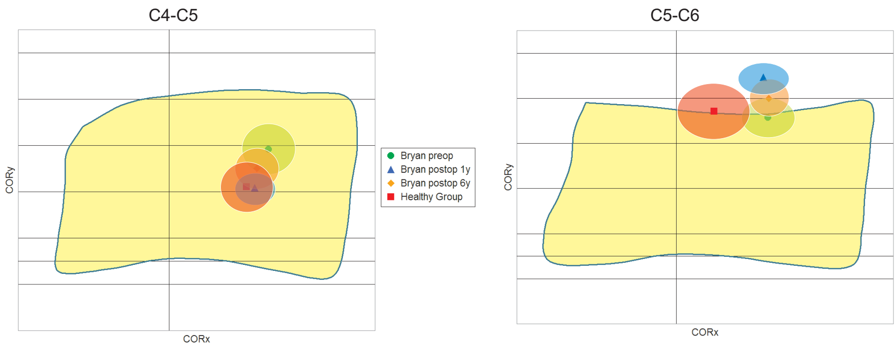

Figure 7.6: Mean (+/- standard deviation) center of rotation based on full flexion and extension positions for the Bryan group (preoperatively, 1 and 6 years postoperatively) and the healthy control group for levels C4-C5 and C5-C6 (index level). The ellipsoid around the mean location illustrates one standard deviation from the mean.

not subjected to abnormal stresses [19]. Similar to the observations of Powell et al. [20], the COR seemed to shift cranially and was less variable with respect to the preoperative situation, although not reaching statistical significance. Unlike Powell et al., no posterior shift of the COR was seen.

Next, to assess whether the maintained motion of the Bryan group was physiological and normal, motion patterns of the Bryan cohort at 1 and 6 years after surgery were compared to those of an age- and disc-degeneration-matched healthy control group. Both the age and the radiological disc degeneration of the Bryan group at the preoperative situation did not differ from healthy control group. The ROM results of the healthy control group for flexion/extension lay within the broad range of ROM values previously reported in literature [8, 17, 22, 31]. This is also true for AP translation [8] and the COR [6, 17, 1]. It is difficult to compare CAM with historical results, as only few of them are available in literature today. Only Goffin et al., Van Mameren et al., and Wu et al. reported reliable data [11, 32, 16]. Our results correlate well with their findings. Only Wu et al. reported on continuous AP translational motion [32]. As our translation results were normalized to the width of the vertebral body [8], a direct comparison with their results was not possible; the trends are however similar.

Our results suggest that the prosthesis is able to mimic normal ROM, CAM and the COR at 1 or 6 years after surgery as no significant differences were found when comparing the Bryan group with the age-matched healthy control group. This is in contradiction with the findings of Rousseau et al. with the Prestige

LP (Medtronic, Memphis, TN) and the Prodisc-C (Synthes, West Chester, PA) [23]. They compared ROM and COR with a control group of 200 healthy discs and found that ROM was significantly reduced with both prostheses and that the COR was significantly influenced by the type of prosthesis. The COR trended to be located more anterior and superior than normal. In our study with the Bryan Cervical Disc prosthesis, the COR was located more posterior and superior, although not significantly.

For the Bryan patients AP translation and CTM can not be considered normal as they significantly differed from the values found in our age-matched healthy control group. Like the variation in the COR, the variation in AP translation and CTM was slightly reduced after insertion of the prosthesis. This might indicate that the prosthesis restricts or limits translation during flexion/extension.

Interestingly, the qualitative motion patters of the index level were at 6 years postoperatively better correlated to the healthy control group than at 1 year postoperatively. The coefficients of multiple determination increased from 0.92 to 0.95 for CAM and from 0.77 to 0.80 for CTM. The COR at 6 year postoperatively was significantly closer to the COR of the healthy control group than at 1 year after surgery. This might indicate that the spine needs time to adapt after insertion of the prosthesis and might eventually evolve towards the restoration of physiological normal motion. A similar, however slower, evolution process after cervical arthroplasty can be seen with heterotopic ossification (HO). In a long term radiological follow-up study, Walraevens et al. observed that HO developed during the first four postoperative years, but increased only minimally and not significantly when comparing 4 years to 8 years follow-up [30]. In this study, 94% of the patients who were HO free at 4 years after surgery remained HO free up to 8 years postoperative. This observation might confirm the hypothesis that the cervical spine adapts to the changed biomechanics after cervical arthroplasty prior to stabilizing its motion patterns.

A possible limitation of this study is the small number of patients in the Bryan cohort and the healthy control group. Small sample size can introduce large variations and could mask differences between groups [20]. Moreover, intervertebral motion of C6-C7 was not investigated in this study as this level was frequently not visible on the fluoroscopic image sequences. Nevertheless, C6-C7 is operated upon commonly [26, 14, 12] and should therefore be investigated in upcoming studies. Finally, our study did not look at lateral bending and axial rotation. As both lateral bending as axial rotation are routinely performed during daily functional tasks [4], they should be addressed in future studies.

7.5 Conclusion

The results of this study indicate that the Bryan prosthesis is able to maintain motion with respect to the preoperative situation, both in quantity as in quality, up to 6 years after surgery. Moreover, the prosthesis is able to mimic normal intervertebral ROM, angular motion and a physiological center of rotation. The prosthesis does however not allow normal AP shear and translation. Finally, it might be hypothesized that the cervical spine adapts to the changed biomechanics after cervical arthroplasty prior to stabilizing its motion patterns.

Acknowledgments

Medtronic (TN, USA) is gratefully acknowledged for the institutional research and education grant. Philippe Demaerel, MD, PhD, is acknowledged for his contribution of the radiological imaging. Paul Suetens, PhD, is acknowledged for the co-development of the motion analysis tool. Jan Leemans and Guido Pauwels are gratefully acknowledged for their technical contribution during imaging.

Author's involvement

All authors, Joris Walraevens, Jos Vander Sloten, PhD, Johan van Loon, MD, PhD, Frank Van Calenbergh, MD, and Jan Goffin, MD, PhD, were substantially involved in this multidisciplinary research. All radiological data was collected by Joris Walraevens and Jan Goffin. Disc replacement surgeries were performed by Jan Goffin, Johan van Loon, and Frank Van Calenbergh. The data analysis was performed by Joris Walraevens and was supervised by Jos Vander Sloten and Jan Goffin. This manuscript was written up by Joris Walraevens and was reviewed by all authors.

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Chapter 8

Postoperative segmental malalignment after surgery with the Bryan Cervical Disc Prosthesis: is it related to the mechanics and design of the prosthesis?

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Adapted from a manuscript published in J of Spinal Disord Tech 23(6):372-376 (2010)

Abstract

Study design In a radiographic study, postoperative segmental alignment was compared between two cohorts of 20 consecutive patients operated with a Bryan Cervical Disc Prosthesis. In group II, patients with severe preoperative kyphosis were excluded for disc replacement surgery and the surgical technique was slightly altered in order to avoid asymmetric overdrilling of the posterior part of the cranial endplate of the caudal vertebral body.
Objective The aim was to investigate whether the change in patient inclusion criteria and the modification of the surgical technique had an influence on postoperative segmental alignment, and whether postoperative kyphosis is related to the mechanical properties and/or the design of the prosthesis.
Summary of Background data Several research groups reported segmental kyphosis after treatment of degenerative disc disease with the Bryan Cervical Disc Prosthesis.
Methods Based on lateral radiographs, the disc insertion angle (as a postoperative estimate for the intraoperative angle of approach), the angle of the functional spinal unit (FSU) and disc angle (both as measures for segmental alignment) were calculated.
Results In group I, 80% of the patients had a kyphotic FSU angle and 40% had a kyphotic disc angle preoperatively. At follow-up, 65% of the patients had a kyphotic FSU angle while 55% had a kyphotic disc angle. In group II, 40% of the patients had a kyphotic FSU angle and 5% had a kyphotic disc angle preoperatively. At follow-up, 40% of the patients had a kyphotic FSU angle while 5% had a kyphotic disc angle.
Due to the change in patient inclusion criteria, there was a significant difference in preoperative FSU angle between group I and group II; however no significant difference in preoperative disc angle was found. Due to the change in surgical technique, the disc insertion angle was significant different between both groups. A difference in postoperative FSU angle, however nonsignificant, between both groups was observed. There was a significant difference in postoperative disc angle between both groups; group I showed significantly more kyphosis of the shells than group II.
Conclusions This study shows that segmental malalignment with the Bryan Disc can be reduced and is therefore not device related. Proper patient selection and a modified surgical technique can prevent this adverse outcome.

8.1 Introduction

The Bryan Cervical Disc Prosthesis (Medtronic, Memphis, USA) is one of the earliest and widely used prostheses for cervical disc replacement. Various intermediate-term follow-up studies have reported promising clinical and radiological results after treatment of degenerative disc disease [1, 6, 5, 13, 19]. Over the past two years however, several research groups reported postoperative kyphosis at the treatment level after surgery [3, 8, 15, 12, 16]. The question rose whether this postoperative kyphosis is related to the mechanical properties and/or the design of the prosthesis or to other biomechanical and surgical factors.

An analysis of the first consecutive series of patients operated with the Bryan Cervical Disc Prosthesis [6] showed several cases of postoperative kyphosis. Taking these early results into account, it was hypothesized that preoperative segmental alignment and surgical technique might be factors influencing postoperative alignment at the index level [12, 3, 18] and therefore future patients with severe preoperative kyphosis were excluded for disc replacement surgery and the surgical technique was slightly altered in order to avoid asymmetric overdrilling of the posterior part of the cranial endplate of the caudal vertebral body.

The aim of this study is to investigate whether this change in patient inclusion criteria and this modification of the surgical technique had an influence on postoperative segmental alignment after surgery with a Bryan Cervical Disc Prosthesis, with an ultimate goal to determine whether postoperative kyphosis is related to the mechanical properties and/or the design of the prosthesis.

8.2 Materials and methods

In a radiographic study, two groups of patients were compared: a cohort of twenty consecutive patients operated upon between 2000 and 2001 (group I) and a cohort of twenty consecutive patients operated upon between 2005 and 2007 (group II). Group I patients were part of a prospective European multicenter trial of which the one- and two-years results have been published [5, 6]. All group I and II patients were operated by the last author and had a preoperative diagnosis of symptomatic cervical disc degeneration with or without spondylosis, causing radiculopathy and/or myelopathy.

Range of motion (ROM) of the index level is defined as the intervertebral sagittal rotation between full flexion and extension. Preoperative and postoperative ROMs were measured on dynamic lateral radiographs in both groups. Segmental alignment was assessed using the angle of the functional

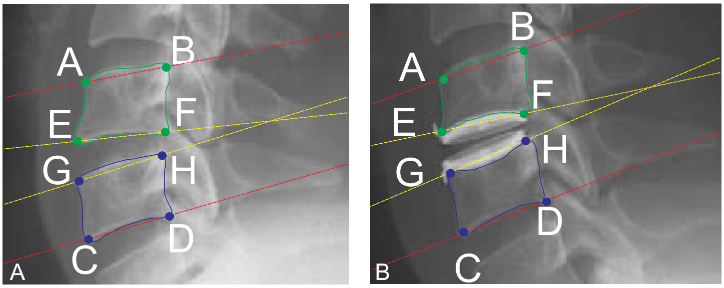

Figure 8.1: The angle of the functional spinal unit (aFSU) is defined as the angle between the superior endplate of the superior vertebral body (AB) and the inferior endplate of the inferior vertebral body (CD). The disc angle is calculated as the angle between the inferior endplate of the superior vertebral body (EF) and the superior endplate of the inferior vertebral body (GH) (figure A) or as the angle formed by superior shell (EF) and the inferior shell (GH) of the prosthesis (figure B).

spinal unit (FSU) and the disc angle. The former is defined as the angle between the superior endplate of the superior vertebra and the inferior endplate of the inferior vertebra (figure 8.1). Preoperatively, the disc angle is the angle between the inferior endplate of the superior vertebra and the superior endplate of the inferior vertebra (figure 8.1a). Postoperatively, it is the angle between the shells of the prosthesis (figure 8.1b).
The surgical technique was slightly modified for the second group compared to the first one in order to prevent overdrilling of the posterior part of the superior endplate of the caudal vertebral body. In group I, the prosthesis was inserted as described in the manufacturer's insertion guide [6, 2] along a line perpendicular to one that connects the superior posterior corner of the superior vertebral body and the inferior posterior corner of the inferior vertebral body (figure 8.2a). In group II, the prosthesis was inserted along a line parallel to the superior endplate of the caudal vertebral body at the implanted level (figure 8.2b). The disc insertion angle (aDI) was used as a postoperative parameter to assess the intraoperative angle of approach. The disc insertion angle is defined as the angle between the bisector between the shells of the prosthesis and the line connecting the posterior superior corner of the superior vertebra with the posterior inferior corner of the inferior vertebral body (figure 8.3).
All radiographic measurements were done using a custom developed image analysis tool (BMGO, KULeuven, Belgium), which has a measurement error of 0.3° and 0.3 mm and excellent inter- and intrarater agreement (ICC>0.75). A FSU or disc angle larger than 1° reflected kyphosis, whereas angles lower than -1° denoted lordosis; angles between -1° and 1° were considered neutral.

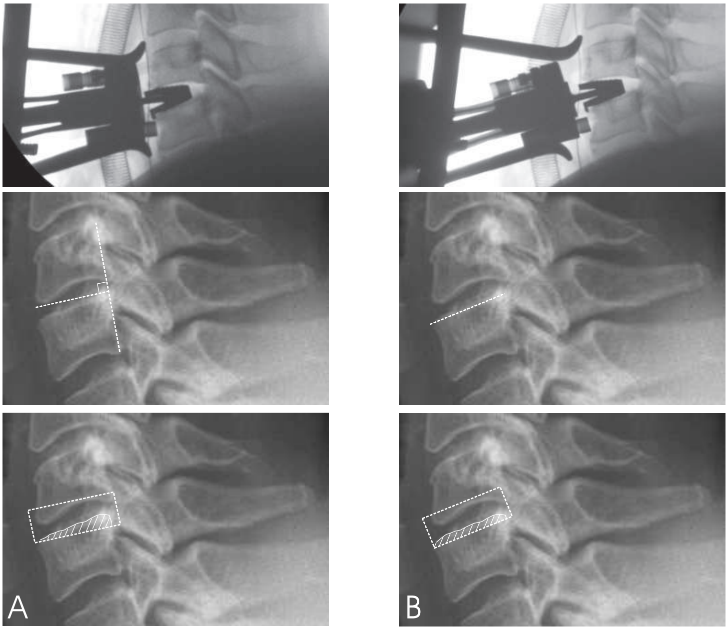

Figure 8.2: (A) In group I, the prosthesis was inserted along a line perpendicular to one that connects the superior posterior corner of the superior vertebral body and the inferior posterior corner of the inferior vertebral body. (B) In group II, the prosthesis was inserted along a line parallel to the superior endplate of the caudal vertebral body at the implanted level to prevent overdrilling of the posterior part of the superior endplate of the caudal vertebral body.

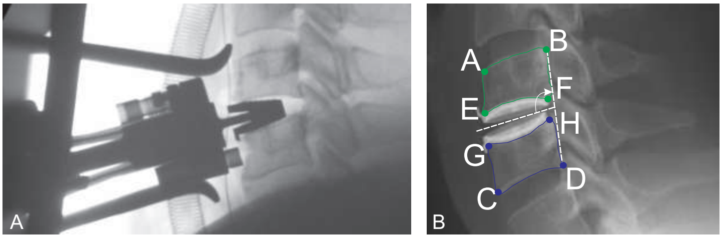

Figure 8.3: The postoperative disc insertion angle is defined as the angle between the bisector of the shells (dashed line) and the line that connects the superior posterior corner of the superior vertebral body and the inferior posterior corner of the inferior vertebral body (BD).

Statistical Analysis

A p-value of 0.05 was considered significant. Linear correlations were investigated using the Spearman r correlation coefficient. A Student t-test was used to compare both groups if the data was Gaussian and continuous. In other situations, a Mann-Whitney U-test was used.

8.3 Results

Patients in both groups were comparable in terms of age and preoperative and postoperative ROM ($p>0.05$).
In group I, 80% of the patients had a kyphotic FSU angle and 40% had a kyphotic disc angle at the preoperative situation. At follow-up, 65% of the patients had a kyphotic FSU angle while 55% had a kyphotic disc angle. One patient had a kyphotic FSU and disc angle at follow-up while having lordotic angles at baseline. The mean change between postoperative and preoperative FSU angle was -0.6+/-6.3°. A significant positive correlation between preoperative and postoperative FSU angle was found (r: 0.74; $p<0.05$). The mean change between postoperative and preoperative disc angle was 8.1+/-6.3°. No correlation between preoperative and postoperative disc angles was found ($p=0.22$).
In group II, 40% of the patients had a kyphotic FSU angle and 5% had a kyphotic disc angle at the preoperative situation. At follow-up, 40% of the patients had a kyphotic FSU angle while 5% had a kyphotic disc angle. Lordosis was maintained for all patients that were lordotic at baseline. The mean change between postoperative and preoperative FSU angle was -0.2+/-4.8°. Similar to group I, a significant positive correlation between preoperative and postoperative FSU angle was found (r: 0.75; $p<0.05$). The mean change between postoperative and preoperative disc angle was -3.5+/-5.9°. No correlation between preoperative and postoperative disc angles was found ($p=0.31$).
Next, preoperative segmental alignment and surgical technique was compared between both groups. On average, there was a significant difference in preoperative FSU angle between group I and group II ($p<0.05$), however no significant difference in preoperative disc angle ($p>0.05$) was found. Due to the change in surgical technique, the disc insertion angle was significant different between both groups ($p<0.05$).
Finally, postoperative segmental alignment was compared in both groups. A difference in postoperative FSU angle, however nonsignificant due to large intragroup variations, between both groups was observed ($p>0.05$). There was

Table 8.1: Comparison of predictor values and outcome measures for both groups of patients. Results are displayed as means +/- standard deviations. ROM: range of motion, FSU: functional spinal unit. A FSU or disc angle larger than 1° reflected kyphosis, whereas angles lower than -1° denoted lordosis; angles between -1° and 1° were considered neutral.

	Group I	Group II	
General			
Age (y)	55+/-9	51+/-12	p>0.05
Preop ROM (°)	10.3+/-5.1	11.0+/-5.6	p>0.05
Postop ROM (°)	8.9+/-5.4	10.6+/-3.9	p>0.05
Predictors			
Preop FSU angle (°)	5.8+/-8.1	-0.1+/-6.6	p<0.05
Preop disc angle (°)	-1.5+/-6.0	-3.4+/-3.5	p=0.28
Disc insertion angle (°)	91.7+/- 2.0	93.8+/-2.0	p<0.05
Outcome measures			
Postop FSU angle (°)	3.6+/-8.0	0.1+/-7.2	p=0.17
Postop disc angle (°)	2.6+/-6.8	-6.7+/-3.9	p<0.05

however a significant difference in postoperative disc angle between group I and group II; group I showed significantly more kyphosis of the shells than group II ($p<0.05$).
All results are summarized in table 8.1.

8.4 Discussion

In contrast to various promising clinical and radiographic results [5, 6, 11], postoperative segmental kyphosis after surgery with a Bryan Cervical Disc Prosthesis has been reported in literature [20, 9]. Fong et al. found several cases with postoperative kyphosis of the functional spinal unit after surgery with a Bryan Cervical Disc Prosthesis [3]. Pickett et al. reported that the angle of the functional spinal unit became more kyphotic after surgery with the same prosthesis with a mean change of 6° in 50% of all cases (7 of 14 patients); the disc angle lost on average 3.8° of lordosis [12]. Sears et al. reported a series of 67 consecutive patients undergoing 88 cervical disc replacements with the Bryan Cervical Disc Prosthesis. They found a median loss of lordosis of the functional spinal unit of 2° [15]. Kim et al. reported that only 36% of the patients with segmental lordosis at the preoperative situation remained lordotic at 6 to 33 months after surgery with the Bryan Cervical Disc Prosthesis. However, they also noted that preoperatively kyphotic functional spinal units became lordotic in 13% of the patients at the same follow-up point [10].

From a biomechanical point of view, postoperative kyphosis is not negligible. Several authors demonstrated that kyphosis in the cervical spine is one of the factors promoting degeneration of the adjacent intervertebral levels after arthroplasty or anterior cervical fusion [12, 9]. Moreover, it can be hypothesized that kyphosis leads to an accelerated wear of the prosthesis. Indeed, during flexion, prosthetic edge impingement might occur in a kyphotic prosthesis. Edge impingement will have enormous wear implications and should therefore be avoided.

As a consequence, discussion was triggered whether postoperative kyphosis of the index level is device related or if other biomechanical or surgical factors contributed to this phenomenon. In the present study, postoperative segmental alignment of two groups of patients was analyzed and compared. The effect of preoperative alignment and surgical technique as predictors for postoperative alignment was investigated. Two variables were used to describe segmental alignment: the angle of the functional spinal unit and the disc angle. This methodology was chosen, as several cases showed kyphotic angles of the shells, in spite of lordotic functional spinal units (figure 8.4).

An analysis of the first consecutive cohort of 20 patients, group I, showed several cases of postoperative kyphosis: at follow-up, 65% of the group I-patients had a kyphotic FSU angle and 53% had a kyphotic disc angle at the index level. Taking these results into account, it was then hypothesized that preoperative segmental alignment and surgical technique might influence postoperative segmental alignment [3, 12, 18] and for that reason, future patients with severe preoperative kyphosis were excluded for disc replacement surgery and the surgical technique was slightly altered. In group II, 40% of the patients had a kyphotic FSU angle at baseline in contrast to 80% of the patients in group I. On average, group I-patients had a kyphotic FSU angle, whereas group II-patients had a lordotic FSU angle at the preoperative situation. Moreover, in group II solely 5% of the patients had a kyphotic disc angle at baseline in contrast to 40% of the patients in group I.

In group I, the prosthesis was inserted as described in the manufacturer's insertion guide [2, 6], along a line perpendicular to one drawn along the posterior margins of the two vertebral bodies. For all patients of group II, the disc was inserted along a line parallel to the superior endplate of inferior vertebral body at the implanted level, to prevent excessive drilling of the posterior part of the superior endplate of the caudal vertebral body. Surgical techniques comparable to the aforementioned technique have been described previously [12, 4, 7, 17, 21]. Xu et al. used an angle of approach parallel to the angle of the native disc space to avoid asymmetric milling of the endplates. They found no cases of postoperative kyphosis [18]. In this study, the change

Figure 8.4: Patient with a lordotic angle of the functional spinal unit, while having a kyphotic disc angle.

in surgical technique is reflected by the difference in the disc insertion angle between groups I and II. The disc insertion angle is used as a postoperative measure for the intra-operative angle of approach. For group I, the disc insertion angle was –as required by the manufacturer's insertion guide- not significantly different from 90° (figure 8.5a). For group II, the change in surgical technique resulted in a significantly higher disc insertion angle (figure 8.5b).
The alteration in patient selection criteria and modification of the surgical technique led to a reduction of postoperative kyphosis of functional spinal unit and a significant reduction of postoperative kyphosis of the disc. On average, group II-patients showed no loss of lordosis at the index level, but in contrast to others [14, 12], we found a small gain in lordosis for the FSU angle (-0.2°)

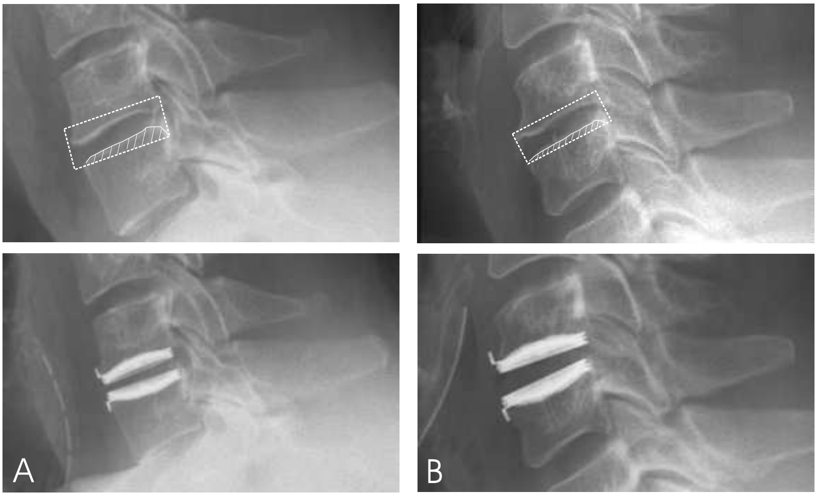

Figure 8.5: In case (a) the prosthesis was inserted as described in the manufacturer's insertion guide along a line perpendicular to one drawn along the posterior margins of the two vertebral bodies leading to overdrilling of the posterior part of the cranial endplate of the caudal vertebral body. In case (b), the disc was inserted along a line parallel to the superior endplate of inferior vertebral body at the implanted level.

and disc angle (-3.3°). Moreover, group II had on average a neutral FSU angle and a lordotic disc angle. The difference between the postoperative angle FSU angles was not significant between both groups due to the large intragroup variations (8.0° for group I and 7.2° for group II). For group I, the FSU angle ranged from 19.0° (kyphosis) to -10.5° (lordosis). For group II, this interval was considerably smaller: it ranged from 11.2° (kyphosis) to -11.5° (lordosis). In group II, 40% of the patients had a kyphotic FSU angle at follow-up in contrast to 65% of the patients in group I. Moreover, in group II 5% of the patients had a kyphotic disc angle at follow-up in contrast to 55% of the patients in group I. The strong correlation between preoperative and postoperative FSU angle confirms the hypothesis that postoperative FSU angle is influenced by the preoperative FSU angle [20, 21, 17].
This study was limited to the assessment of lateral radiographs focusing on postoperative segmental alignment. The impact of malalignment on clinical outcome remains unsolved. Long term follow-up of patients with malalignment and the investigation of a possible correlation between radiographic malalignment and clinical outcome are needed in further studies.

8.5 Conclusion

In contradiction to what is suggested by some authors [15, 12, 9, 20], this study shows that segmental malalignment with the Bryan Cervical Disc Prosthesis can be reduced and is therefore not device related. Proper patient selection and a modified surgical technique can prevent this adverse outcome.

Acknowledgments

Medtronic (Memphis, USA) is acknowledged for the institutional research and education grant.

Author's involvement

All authors, Joris Walraevens, Baoge Liu, MD, Jos Vander Sloten, PhD, and Jan Goffin, MD, PhD, were substantially involved in this multidisciplinary research. All radiological data was collected by Joris Walraevens and Baoge Liu. The data analysis was performed by Joris Walraevens and was supervised by Jos Vander Sloten and Jan Goffin. This manuscript was written up by Joris Walraevens and Jan Goffin and was reviewed by all authors.

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Chapter 9

Influence of a suboptimally placed intervertebral disc prosthesis on the biomechanics of the cervical spine *A radiographic and finite element approach*

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To be submitted for publication in J of Spinal Disord Tech

Abstract

Introduction The goal of this study is twofold. First, the postoperative in vivo placement of a cervical disc prosthesis is quantified in a retrospective radiographic analysis. Next, the influence of a malplaced prosthesis on the biomechanics of the cervical spine is investigated using a finite element model.
Methods In a retrospective analysis, the postoperative positions of Bryan Cervical Disc prostheses were analyzed on AP and lateral radiographs in a cohort of 87 patients. On AP radiographs out-of-midline placement (OM) and coronal tilt (CT) were measured. On lateral radiographic radiographs the gap between the anterior rim of the prosthesis and the vertebral bodies (GAP) and the disc insertion angle (aDI) were obtained. All measured parameters were compared to a perfectly placed prosthesis as advised by the manufacturer (OM=0mm; CT=0°; GAP=0 mm; aDI=90°).
Next, a three dimensional, non-linear, osseoligamentous model of the cervical spine (C2-C7) with a Bryan Cervical Disc prosthesis at C5-C6 was developed. Using this model, the influence of different suboptimal positions of the prosthesis, i.e. OM, CT, GAP, aDI, were investigated. Intervertebral rotations and anteroposterior (AP) translations at the index and adjacent levels as well as the maximum stress in the intervertebral discs and the mean contact forces in the facet joints were analyzed and compared to a model with a degenerated disc at C5-C6.
Results The radiographic analysis showed that postoperative in-vivo positions of the prosthesis significantly deviated from a perfect position for all parameters except for GAP. The parameters were: OM= 1.3 ± 1.1 mm, CT= $2.9 \pm 2.1°$, GAP= 0.4 ± 0.5 mm, aDI= $2.9 \pm 2.0°$, on average.
The finite element analyzes indicated that, with respect to a degenerated model, the introduction of a prosthesis had a considerable effect on the mobility at the index level: it increased with 41-59%. Mobility at the adjacent levels decreased by 10-20%. The position of the prosthesis, i.e. OM, CT, GAP and aDI, had no effect on the mobility of the vertebrae and the stresses in the nuclei. A malplaced prosthesis did however increase the contact forces in the facet joints at the operated level up to 20 N, especially with OM during lateral bending.
Conclusions Optimal placement as advised by the manufacturer was not always obtained in our cases. Nevertheless these malplacements have a negligible influence on the mobility at the index and adjacent levels, on the stresses at the intervertebral discs, and on the contact forces at the facet joints of the adjacent levels. However at the operated level contact forces at the facet joint tend to increase if a prosthesis is not correctly positioned. This might lead to accelerated facet joint degeneration at that level in the future.

9.1 Introduction

During the last decades, anterior decompression and fusion was and at this point in time still is the treatment of choice when an operation is needed after a diagnosis of intervertebral cervical disc disease with radiculopathy and/or myelopathy [11]. During the past years, intervertebral disc replacement has been proposed as an alternative treatment [2, 5, 27]. It is hypothesized that cervical arthroplasty, in contrast to fusion, preserves movement at the operated level and therefore protects the preoperative biomechanical behavior of the cervical spine [8, 19, 28, 29]. As a consequence overloading of the adjacent levels, which might result in adjacent level disease, might be avoided [16, 42, 7, 1, 41].
Up till now, when investigating the influence of cervical arthroplasty on the biomechanics of the cervical spine, a perfect placement of the prosthesis has been assumed. Manufactures consider it to be important that the prosthesis is placed according to their guidelines, as perfect placement would be imperative for a good functionality of the prosthesis [18, 23]. Malplacement might predispose to asymmetric loading, risking premature implant wear, implant loosening, and nonphysiological stresses on adjacent segments and facet joints [22]. Moreover, it is not known what the long term clinical consequences may be of deviations from the manufacturer's recommended 'perfect' positioning of the prostheses [24].
Because of limited intra-operative visibility and work space, a perfect placement is not easy to achieve. As a consequence, despite of navigation tools like fluoroscopy [20, 30, 35] and custom surgical tools [16, 33], perfect placement can not always be guaranteed [20, 30]. Few studies have investigated the accuracy of cervical disc prosthesis placement in surgical practice [3]. Because of the lack of detailed biomechanical data and long term clinical results, little is known about the influence of a suboptimally placement of the prosthesis on the biomechanical behavior of the cervical spine [20, 24].
The goal of this study is twofold. First, immediate in vivo postoperative positions of cervical disc prostheses are quantified in a retrospective study based on lateral and anteroposterior (AP) radiographs. These positions were compared to a perfectly placed prosthesis as advised by the manufacturer. Next, the influence of a malplaced prosthesis on the biomechanics of the cervical spine is investigated using a three dimensional nonlinear finite element model.

9.2 Materials and methods

9.2.1 Radiographic assessment of prosthesis malplacement

In a retrospective study, the immediate postoperative positions of Bryan Cervical Disc prostheses (Medtronic, Memphis, USA) were analyzed on AP and lateral radiographs in a cohort of 87 consecutive single-level patients. Each of the 87 patients was preoperatively diagnosed with cervical intervertebral disc degeneration with radiculopathy and/or myelopathy and received one Bryan Cervical Disc prosthesis (C3-C4: 1 patient, C4-C5: 2 patients, C5-C6: 35 patients en C6-C7: 51 patients) using the Generation I instrument set (Medtronic, Memphis, USA). Each patient was treated at the University Hospital Gasthuisberg, Leuven, Belgium. The total patient population is identical to the single-level cases of the detailed clinical study by Goffin et al. [17] and radiographic study by Walraevens et al. [36]. In total 87 lateral and 53 AP immediate postoperative radiographic, with the patients in an upright position, scans were analyzed.
On AP radiographs two placement parameters were investigated: out-of-midline placement (OM) and coronal tilt (CT). OM, measured in millimeters, was calculated by measuring the distance between the geometric center of the prosthesis relative to a line connecting the geometric centers of cranial and caudal processes spinous (figure 9.1 A). To cope with a possible rotation in the x-ray angle with respect to the true sagittal plane of the vertebral bodies, OM was also determined by measuring the perpendicular distance between the geometrical center of the prosthesis and the plumb line of the uncovertebral joints [3]. If both measurements differed more than 0.5 mm, the latter was retained. CT, measured in degrees, was calculated by measuring the angle between the bisector between the shells of the prosthesis and a line connecting the geometric centers of cranial and caudal spinous processes (figure 9.1 B).
On lateral radiographs, two placement parameters were analyzed: the gap between the anterior rim of the prosthesis and the vertebral bodies (GAP) and the disc insertion angle (aDI). GAP, measured in mm, was determined by measuring the distance between the cranial anterior rim of the prosthesis and the anterior cortical edge of the cranial vertebra, respectively the caudal anterior rim of the prosthesis and the anterior cortical edge of the caudal vertebra (figure 9.2 A). These distances were measured parallel to the orientation of the shells of the prosthesis. The smallest of these 2 distances was retained. aDI, measured in degrees, is used to postoperatively determine the intra-operative angle of insertion of the prosthesis [37]. This angle was calculated as the angle between the bisector of the 2 titanium shells and the line connecting the posterior superior corner of the cranial vertebra with the posterior inferior corner of the caudal vertebra (figure 9.2 B) [25, 32].

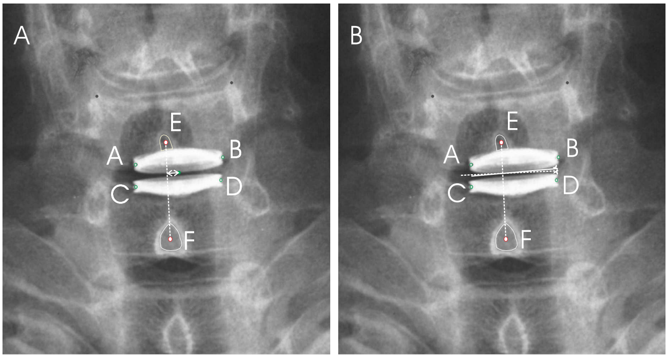

Figure 9.1: (A) Out-of-midline (OM) placement was calculated by measuring the distance between the geometric center of the prosthesis relative to a line connecting the geometric centers of cranial and caudal processes spinous. (B) Coronal tilt (CT) was calculated by measuring the angle between the bisector between the shells of the prosthesis and a line connecting the geometric centers of cranial and caudal processes spinous. Both parameters were calculated on AP radiographs

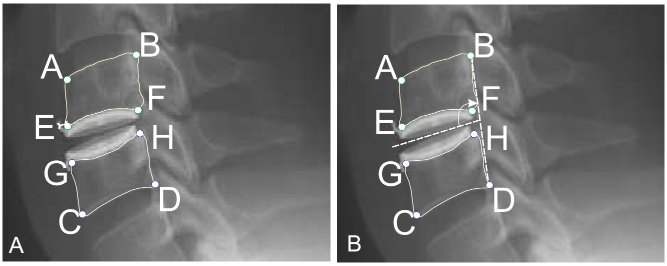

Figure 9.2: (A) The gap between the anterior rim of the prosthesis and the vertebral bodies (GAP), measured in mm, was determined by measuring the distance between the cranial anterior rim of the prosthesis and the anterior cortical edge of the cranial vertebra, respectively the caudal anterior rim of the prosthesis and the anterior cortical edge of the caudal vertebra. These distances were measured parallel to the shells of the prosthesis. The smallest of these 2 distances was retained. (B) The disc insertion angle (aDI), measured in degrees, was calculated as the angle between the bisector of the 2 titanium shells and the line connecting the posterior superior corner of the cranial vertebra with the posterior inferior corner of the caudal vertebra. Both parameters were calculated on lateral radiographs.

The measurement error (ME) [4] and intra-rater agreement, calculated using the intraclass correlation coefficients (ICC) with measures of absolute agreement [34], of the analyzes were assessed by calculating all four parameters three times based on the radiographs of a randomized and blinded subcohort of 30 patients .
A prosthesis was considered 'perfect', if the prosthesis was placed according to the manufacturer's guidelines:

- on the midline of the vertebral bodies in the coronal plane (OM=0 mm)
- without coronal rotation (CT=0°)
- without a gap between the anterior rim of the prosthesis and the cranial or caudal vertebral bodies (GAP=0 mm)
- along the Bryan angle [6, 15, 32] (aDI=90°)

9.2.2 Finite element analysis of prosthesis malplacement

A three dimensional, non-linear, osseoligamentous model of the cervical spine (C2-C7) was used in the finite element analyzes. A Bryan Cervical Disc prosthesis was modeled at C5-C6 (figure 9.3).
The geometry of the model is based on a MRI of a 29-year old male. The vertebral bodies were modeled as rigid bodies. The anterior longitudinal ligament (ALL) and the posterior longitudinal ligament (PLL) were modeled using bilinear membrane elements. The flaval ligaments (FL), the interspinous ligaments (ISL) and the capsular ligaments (CL) were modeled using tension-only bilinear bar elements. The annulus was modeled using homogenized orthotropic cubic solid elements. The nucleus was modeled using nearly incompressible cubic solid elements. The mechanical and material properties of the different structures were adapted from the literature [39, 43, 12]. The Bryan Cervical Disc prosthesis was modeled using tetrahedral solid elements for the nucleus and the titanium (Ti) shells. To simulate the ingrowth of the shells in the bone, the shells were considered glued to the vertebral bodies. Table 9.1 summarizes the geometric and mechanical properties used for the different elements in the model. The model without prosthesis was validated against literature data, both kinematically as well as kinetically. When applying a pure moment of 2 Nm around the three anatomical axes, intervertebral rotations from C2-C3 to C6-C7 lay within the validation corridors reported by Wheeldon et al. [38, 39]. Moreover, using a similar approach, the locations of the centers of rotations are identical to those reported by Dvorak et al. [9, 10],

indicating that the model does not only mimic the quantity but also the quality of intervertebral motion. Finally, the intradiscal pressures in the center nuclei compare well to the values reported in a cadaveric study by Pospiech et al. [26] when pure moments round the different anatomical axes were applied, illustrating the dynamic biofidelity of the model.

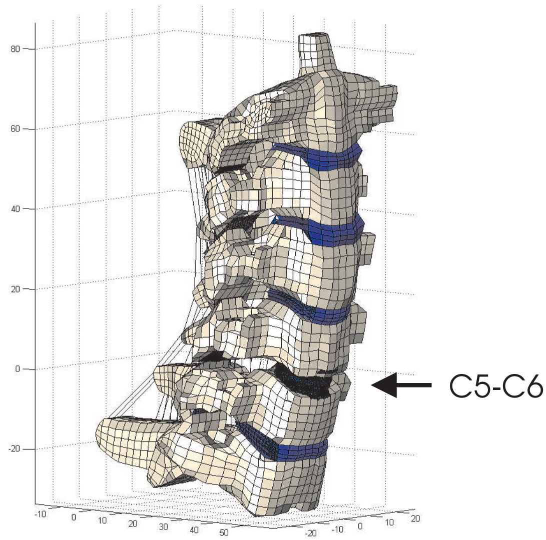

Figure 9.3: A three dimensional, non-linear, osseoligamentous, finite-element model. A Bryan Cervical Disc prothesis was modeled at C5-C6

Using this model, the influence of different suboptimal positions of the prosthesis on the biomechanical behavior of the spine were investigated. In total, four different types of suboptimal placements were considered: out-of-midline placement, coronal tilt of the prosthesis, a gap between the anterior rim of the prosthesis and the vertebral bodies and a deviation from the Bryan angle. For each of these four parameters three different gradations were modeled. The twelve models were compared to (1) a model with an optimally placed prosthesis, (2) a healthy model of the cervical spine without prosthesis and (3) a model of the cervical spine with disc degeneration at C5-C6 but without prosthesis. This last model had a C5-C6 intervertebral disc of which the height was reduced to 50% compared to the healthy model to represent narrowing of the disc space. The intermodel comparison was done for flexion/extension, lateral bending and axial rotation. While C7 was fixed, the loading conditions were applied on C2 using a hybrid loading protocol [14]: a stepwise moment

Table 9.1: Geometric and mechanical properties of the different elements in the finite element model of the cervical spine. E is the Young's modulus, ν is the poisson ration, and μ is the friction coefficient. ISL: intraspinous ligament, CL: capsular ligament, FL: flaval ligament, ALL: anterior longitudinal ligament, PLL: posterior longitudinal ligament. †Load displacement curves were recalculated to stress-strain curves.

	Element type	**Mechanical properties**
Vertebrae	Rigid	/
Ligaments	Bars (ISL, CL, FL)	Adapted† from Wheeldon et al. [39]
	Membranes (ALL, PLL)	Adapted† from Wheeldon et al. [39]
Nucleus	Cubic solids	E=3.4 MPa, ν=0.49
Annulus	Orthotropic cubic solids	E_{11}=E_{33}=3.4 MPa, E_{22}=24 MPa, ν=0.4
Facet surface	Low friction cubic solids	E=3.4 MPa, ν=0.3, μ=0.1
Prosthesis nucleus	Tetrahedral solids	E=70 MPa, ν=0.3
Prosthesis Ti shells	Tetrahedral solids	E=110 GPa, ν=0.49

up to +/-2 Nm was applied onto the intact model. The resulting rotation of C2 with respect to C7 was applied to all other models.
In a kinematic analysis, the influence on the mobility, i.e. intervertebral rotations and anteroposterior (AP) translations, of the index and adjacent levels was investigated. In a kinetic analysis, the maximum stress in middle of the intervertebral discs and the mean normal contact forces in the facet joints were examined.
Because of page limitations, only figures and tables from those malplacement parameters which had the predominant effect on the kinematics and kinetics will be presented.

9.2.3 Statistics

A p-value of 0.05 was considered significant. Linear correlations were investigated using the Spearman r correlation coefficient. A Student t-test was used to compare both groups if the data was Gaussian and continuous. In other situations, a Mann-Whitney U-test was used. Linear correlations were investigated using Pearson's correlation test.

Table 9.2: Measurement errors (ME) and intraclass correlation coefficients (ICC) of the in-vivo placement parameters based on a randomized and blinded cohort of 30 patients. OM: out-of-midline, CT: coronal tilt, GAP: gap between anterior rim of the prosthesis and anterior edge of the vertebral body, aDI: disc insertion angle.

	ME	ICC
OM	0.34 (mm)	0.77
CT	0.72 (°)	0.71
GAP	0.21 (mm)	0.72
aDI	0.76 (°)	0.70

9.3 Results

9.3.1 Radiographic analysis

The repeatability of the measurements was good to excellent (ICC>0.70; table 9.2). The measurement errors were low for all parameters (<0.34mm and <0.76°; table 9.2).
Significant deviations compared to a perfectly placed prosthesis, as advised by the manufacturer (OM=0 mm, CT=0°, GAP=0 mm, aDi=90°), were found for OM, CT and aDI (table 9.3; p<0.05). There was no significant difference in GAP. OM was 1.3+/-1.1 mm; CT was 2.9+/-2.2°; GAP was 0.4+/-0.5 mm; and aDI was 92.9+/-2.0° on average.
No significant correlations were found between the different parameters (p>0.05).

Table 9.3: Results obtained with in-vivo placement of Bryan Cervical Disc prostheses in a cohort of 87 patients. OM: out-of-midline, CT: coronal tilt, GAP: gap between anterior rim of the prosthesis and anterior edge of the vertebral body, aDI: disc insertion angle

	Optimal	Cohort	p
OM(mm)	0.0	1.3±1.1	<0.05
CT (°)	0.0	2.9±2.1	<0.05
GAP (mm)	0.0	0.4±0.5	>0.05
aDI (°)	90	92.9±2.0	<0.05

9.3.2 Finite element analysis

Compared to the model with intervertebral disc degeneration at the target level C5-C6, motion of a perfectly placed Bryan Cervical Disc prosthesis increased with 41-59% while the mobility of the other levels decreased with 10-20%, during lateral bending, axial rotation and extension-flexion (tables 9.4, 9.5, 9.6, and 9.7). Compared to the healthy model, mobility of the operated level increased with 12-17% while the mobility of the other levels decreased with 6-13%. At the adjacent levels, i.e. C4-C5 and C6-C7, the stresses in the intervertebral discs decreased by 20-30% (e.g. figure 9.4) and that the contact forces in the facet joints decreased with 30% to 50% (e.g. figure 9.5) compared to the degenerated model. Stresses in the intervertebral discs of the adjacent levels decreased by 14-19% and the contact forces in the facet joints decreased with 21% to 35% compared to the healthy model.
A suboptimally placed prosthesis did not influence the kinematics of the cervical spine compared to a perfectly placed prosthesis. Both the intervertebral rotations (e.g. figure 9.6) and translations (e.g. figure 9.7) remained unaltered despite of the different gradations of OM, CT, GAP, and aDI (tables 9.4, 9.5, 9.6, and 9.7; $p>0.05$). Moreover there were no differences in stress in the intervertebral discs at the adjacent non-instrumented levels due to prosthesis malplacement for any of the parameters (e.g. figure 9.4). Likewise the placement of the prosthesis had no influence on the contact forces in the facet joints of the non-operated levels despite of the different gradations of OM, CT, GAP, and aDI (e.g. figure 9.5). However, at the operated level there were increases in facet contact forces, up to 20 N (+333%), especially during lateral bending with a prothesis that is positioned out-of-midline and during extension with a prosthesis that has a gap between the anterior rim of the prosthesis and the anterior edge of the vertebral body. aDI and CT had little influence on facet contact force at the index level.

Table 9.4: Contribution (in %) of each intervertebral level to the global ROM of the cervical spine (C2-C7) during left and right lateral bending with a prosthesis implanted out-of-midline (OM) at C5-C6

	No prosthesis		OM=0.0mm		OM=1.3mm		OM=2.4mm		OM=3.5mm	
	left	right	left	right	left	right	left	right	left	right
C2-C3 (%)	15.3	15.3	15.0	15.0	15.2	15.0	15.1	14.8	15.0	15.4
C3-C4 (%)	22.4	22.4	17.6	17.6	17.9	17.6	18.9	18.0	19.4	18.1
C4-C5 (%)	26.5	26.5	23.0	23.0	23.9	23.5	23.7	23.3	24.1	23.9
C5-C6 (%)	18.9	18.9	30.5	30.5	28.8	29.9	28.2	29.6	27.5	28.2
C6-C7 (%)	16.8	16.8	13.9	13.9	14.1	13.9	14.1	14.3	14.0	14.4
Total (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Table 9.5: Contribution (in %) of each intervertebral level to the global ROM of the cervical spine (C2-C7) during left and right axial rotation with a prosthesis implanted with coronal tilt (CT) at C5-C6

	No prosthesis		CT=0.0°		CT=2.9°		CT=5.0°		CT=7.1°	
	left	right	left	right	left	right	left	right	left	right
C2-C3 (%)	21.4	21.4	18.1	18.1	18.1	18.2	18.1	18.2	18.1	18.2
C3-C4 (%)	24.1	24.1	22.1	22.1	22.1	21.8	22.1	21.8	22.0	21.8
C4-C5 (%)	20.3	20.3	16.0	16.0	16.0	16.1	16.0	16.1	16.3	16.1
C5-C6 (%)	17.6	17.6	29.5	29.5	29.5	29.8	29.5	29.8	29.4	29.8
C6-C7 (%)	16.6	16.6	14.2	14.2	14.2	14.0	14.2	14.0	14.2	14.0
Total (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Table 9.6: Contribution (in %) of each intervertebral level to the global ROM of the cervical spine (C2-C7) during flexion/extension with a prosthesis implanted with a gap between the anterior rim of the prosthesis shells and the anterior edge of the vertebral bodies (GAP) at C5-C6

	No prosthesis		GAP=0.0mm		GAP=0.8mm		GAP=1.3mm		GAP=1.8mm	
	ext	flex	ext	flex	ext	flex	ext	flex	ext	flex
C2-C3 (%)	18.8	24.0	13.9	23.6	14.6	24.0	14.5	24.0	14.6	24.1
C3-C4 (%)	19.6	19.0	14.6	18.6	14.6	19.0	15.2	19.0	15.3	19.1
C4-C5 (%)	29.7	17.5	20.4	17.1	20.4	17.5	21.7	17.5	21.9	17.6
C5-C6 (%)	23.2	19.0	42.3	20.6	41.6	19.5	39.9	19.0	39.4	18.6
C6-C7 (%)	8.7	20.5	8.8	20.1	8.8	20.0	8.7	20.5	8.8	20.6
Total (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Table 9.7: Contribution (in %) of each intervertebral level to the global ROM of the cervical spine (C2-C7) during left and right lateral bending with a prosthesis implanted with a disc insertion angle (aDI) which deviates from the Bryan angle (aDi=90°) [6, 15] at C5-C6

	No prosthesis		aDI=90.0°		aDI=92.9°		aDI=94.9°		aDI=96.9°	
	left	right	left	right	left	right	left	right	left	right
C2-C3 (%)	15.3	15.3	15.0	15.0	15.1	15.1	15.1	15.1	15.1	15.1
C3-C4 (%)	22.4	22.4	17.6	17.6	17.7	17.7	17.9	17.9	18.4	18.4
C4-C5 (%)	26.5	26.5	23.0	23.0	23.3	23.3	23.7	23.7	24.1	24.1
C5-C6 (%)	18.9	18.9	30.5	30.5	29.9	29.9	29.2	29.2	28.4	28.4
C6-C7 (%)	16.8	16.8	13.9	13.9	14.0	14.0	14.1	14.1	14.0	14.0
Total (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

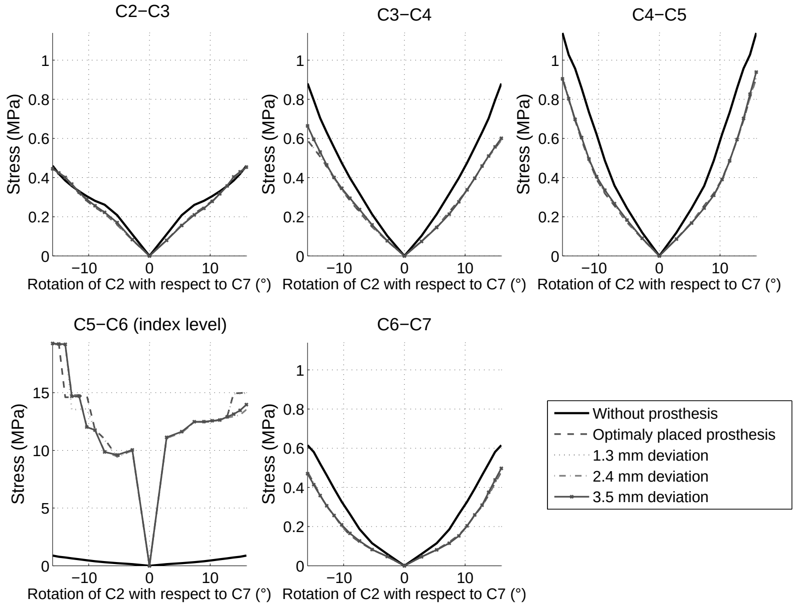

Figure 9.4: Intradiscal pressure during lateral bending based on an intact degenerated model and on models with different variations of out-of-midline placements of a prosthesis at C5-C6. Negative rotation denotes left lateral bending, positive rotation denotes right lateral bending.

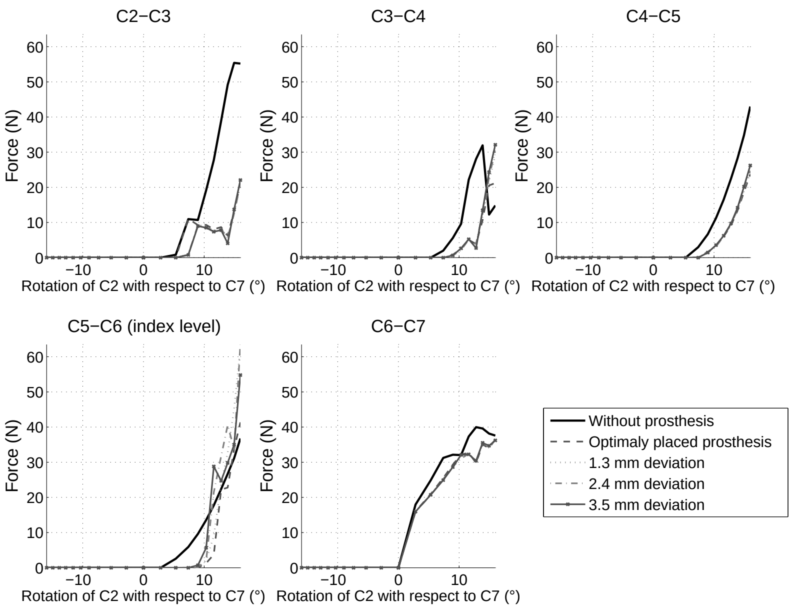

Figure 9.5: Contact forces on the right facet joint during lateral bending based on an intact degenerated model and on models with different variations of out-of-midline placements to the left of a prosthesis at C5-C6. Negative rotation denotes left lateral bending, positive rotation denotes right lateral bending.

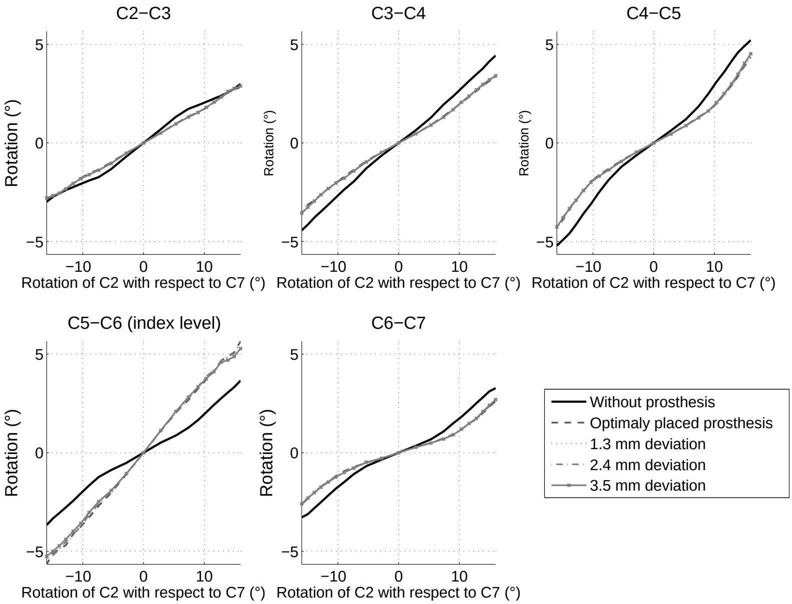

Figure 9.6: Intervertebral angular motion during lateral bending based on an intact degenerated model and on models with different variations of out-of-midline placements of a prosthesis at C5-C6. Negative rotation denotes left lateral bending, positive rotation denotes right lateral bending.

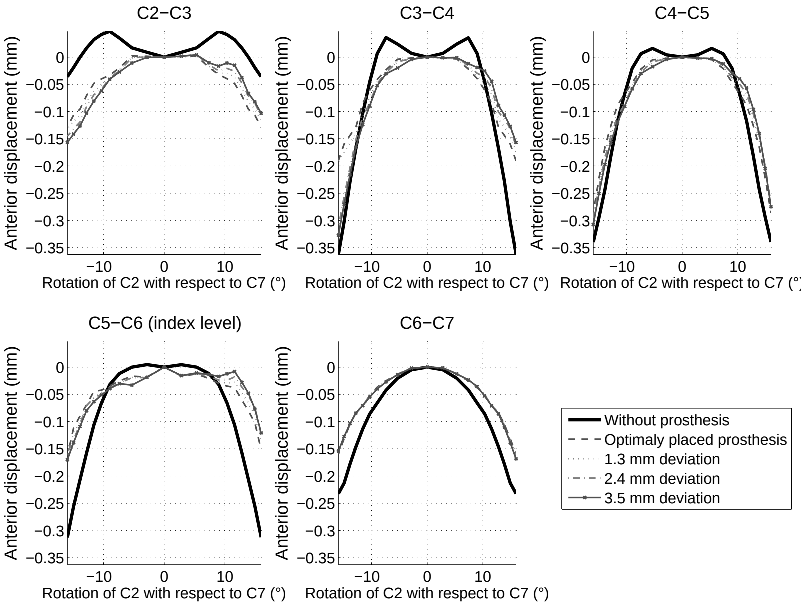

Figure 9.7: Intervertebral anteroposterior translations during lateral bending based on an intact degenerated model and on models with different variations of out-of-midline placements of a prosthesis at C5-C6. Negative rotation denotes left lateral bending, positive rotation denotes right lateral bending. Negative displacement represents posterior translation whereas positive displacement represents anterior translation.

9.4 Discussion

The purpose of this study was twofold. First the surgical accuracy of the placement of cervical disc prostheses was investigated. The retrospective study of radiographs showed in-vivo prosthesis positions which significantly deviated from a perfect position as advised by the manufacturer for OM, CT and aDI. The significant higher aDI might be explained as a modified surgical technique was used from 2002 on, to prevent overdrilling of the posterior part of the superior endplate of the caudal vertebral body. From 2000 to 2002, the prosthesis was inserted as described in the manufacturer's insertion guide [6, 15] along a line perpendicular to one that connects the superior posterior corner of the superior vertebral body and the inferior posterior corner of the inferior vertebral body (aDI=90°). From 2002, the prosthesis was inserted along a line parallel to the superior endplate of the caudal vertebral body at the implanted level. In total, 60 patients were operated following the manufacturer's guidelines. The average aDI of this cohort was 91.2+/-1.8° which does not significantly deviate from the aDI proposed by the manufacturer ($p>0.05$). The remaining 27 patients were operated following the modified surgical technique. The average aDI of the latter cohort was 96.7+/-2.5° and differs significantly from the aDI proposed by the manufacturer ($p<0.05$). However, as it has been shown that the modified surgical technique diminishes the chance on postoperative kyphosis [37], it may be biomechanically and clinically favorable to deviate from the guidelines in some cases.
Our findings are comparable with results from similar studies. Barbagello et al. investigated out-of-midline placement of the ProDisc-C cervical disc prosthesis (Synthes, USA) and found that 31.5% of the implanted prostheses had an out-of-midline placement of more than 2.0 mm, using the standard fluoroscopic technique to mark the midline [3]. In contrast to the lack of biomechanical data for implant position assessment in the cervical spine, several research groups have reported on position assessments in the lumbar spine, mostly using CT scans. Marsham et al. investigated malplacement of the O- and A-Maverick Lumbar Disc (Medtronic, USA) on high-resolution CT scans [21]. They found important out-of-midline (>4 mm) and coronal tilt (>4°) with both devices. Patel et al. found slightly lower values with the Pro-Disc II (Synthes, USA) [24], e.g. out-of-midline placement up to 1.2 mm. These results correlate well with our observed results and illustrate that it is not obvious to place a disc prosthesis 'perfectly'. Therefore user friendly, accurate and non time consuming techniques and surgical tools can be helpful to obtain adequate accuracy for prosthesis placement.

Second, the influence of the introduction and the position of a disc prosthesis on the biomechanical behavior of the cervical spine was studied. The results

show that cervical arthroplasty alters the biomechanics at the index and at the adjacent levels compared to a degenerated, non operated cervical spine. In a retrospective radiography study, Wigfield et al. investigated the influence of a disc prosthesis on the mobility of the spine [40]. Similar to the current results, they found that the mobility of the instrumented level increases. This increase is compensated by the decrease in mobility at non-operated levels. In another study Wigfield et al. conducted a cadaver study to investigate the influence of an intervertebral disc prosthesis on the stresses at the adjacent intervertebral discs [41]. Like the results obtained in our study, they measured that the stresses in the non-operated levels decrease due to the arthroplasty. Using a similar finite element model Goel et al. analyzed the influence of lumbar arthroplasty on the contact forces in the facet joints and found that the forces in the facet joints of the non-operated levels decrease due to implantation of a prosthesis [13]. This finding was also confirmed in our study. The order of magnitude of the contact forces calculated in our models corresponded well with the data from lumbar cadaver experiments by Schendel et al. [31].
The results of our finite element analyzes suggest that the position of the prosthesis has no influence on the mobility of the vertebrae nor on the stresses in the intervertebral discs at the non-operated and operated levels. Malplacement, in terms of OM, GAP, CT and aDI, has no influence on the contact forces in the facet joints at the non-operated levels. However at the operated level an increase in facet contact force was observed during lateral bending with a prosthesis that is positioned out-of-midline and during extension with a prosthesis that has a gap between the anterior rim of the prosthesis and the anterior edge of the vertebral body. A prosthesis with 3.5 mm OM led to an increase in facet contact force of 13 N (+216%). To place this result in perspective, in the retrospective radiographic analysis OM was 1.3 mm on average. In this case, the increase in facet contact force would be limited to 3 N. Nevertheless, one might speculate whether or not a severe increase in facet contact force will lead to accelerated facet joint degeneration and pain in the future. It is therefore recommended to avoid important out-of-midline placement.
These results underline the benefit of finite element analyzes for cervical arthroplasty research. Indeed, facet contact forces are measured with extreme difficulty in vivo and in vitro. Finite element analyzes do provide the possibility to accurately assess and predict these forces.

As a drawback, the FE model was solely validated against literature data. In vitro experiments to further validate this model are required. Moreover, this study did not investigate the influence of the size of cervical disc prostheses nor the impact of a suboptimal position of the prosthesis on clinical outcome. It remains unknown what the critical position accuracy is to obtain proper long-term function of the implant and its influence on clinical outcome.

9.5 Conclusion

Optimal placement as advised by the manufacturer is not always feasible in clinical practice. Although finite element analyzes show that cervical arthroplasty has an influence on the biomechanical behavior of the cervical spine, malplacement of the prosthesis has a negligible influence on the mobility of the index and adjacent levels, on the stresses in the intervertebral discs, and on the contact forces in the facet joints at the adjacent levels. However, at the operated level contact forces in the facet joint tend to increase if a prosthesis is not correctly positioned. This might lead to accelerated facet joint degeneration at that level and neck pain in the future.

Acknowledgments

Medtronic (TN, USA) is gratefully acknowledged for the institutional research and education grant. Bram Lenaerts is acknowledged for his contributions during the finite element analyzes.

Author's involvement

All authors, Joris Walraevens, Jos Vander Sloten, PhD, and Jan Goffin, MD, PhD, were substantially involved in this multidisciplinary research. All data was collected by Joris Walraevens and Jan Goffin. The analyzes were performed by Joris Walraevens and Bram Lenaerts and were supervised by Jos Vander Sloten and Jan Goffin. Disc replacement surgeries were performed by Jan Goffin, Johan van Loon, and Frank Van Calenbergh. This manuscript was written up by Joris Walraevens and was reviewed by all authors.

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Chapter 10

General conclusions and future perspectives

This final chapter starts with a concise summary of the content and a recapitulation of the most important conclusions of this thesis. Subsequently some reflections on the initial stated hypotheses follow. Finally, possible topics for future research are indicated.

10.1 Summary and conclusions

10.1.1 Realization of objectives

Biomechanics of cervical disc prostheses are an interesting, young and multidisciplinary research discipline. If the quest for innovation continues, cervical arthroplasty has the potential to revolutionize the treatment of cervical degenerative disease. But distinct guidelines for favorable patient inclusion criteria in terms of preoperative mobility, pre-existing intervertebral disc degeneration and preoperative alignment, are needed and surgical techniques should optimized to achieve high prosthesis placement accuracy. Through a close collaboration between engineering, medicine and industry, this PhD tried to answer some of the questions regarding cervical disc replacements that were raised in literature.

Chapters 1 and 2 introduced the biomechanical research field of cervical arthroplasty and stated the objectives and underlying hypotheses of this work.

In chapter 3, a motion analysis tool for calculating lateral intervertebral continuous motion patterns in the cervical spine was presented. An existing tool, which has proven its value in over twelve important studies, served as a benchmark in the validation process. The here developed motion tool was highly repeatable and had a similar accuracy compared to the benchmark was achieved in measuring the quantity of intervertebral motion, expressed by the range of motion and anteroposterior translation. Moreover, in contrast to the bench mark technique, the here developed tool was found to be fast and user-undemanding: besides a training set of segmented vertebrae, no input is required, enabling its use in day to day clinical practise.

In chapter 4, two separate objective scoring systems to qualitatively and quantitatively assess the degree of cervical intervertebral disc degeneration on lateral radiographs and facet joint degeneration on CT scans, were developed and validated. It was concluded that both scoring systems fulfilled the criteria for recommendation proposed by Kettler and Wilke and are reliable and objective. Moreover, the scoring system for cervical disc degeneration showed to be experience- and discipline-independent which increases the number of potential users.

Chapter 5 investigated quantitative and qualitative motion patterns of the cervical spine during flexion/extension, lateral bending and axial rotation of asymptomatic volunteers of different ages and looked at possible correlations between disc degeneration and intervertebral motion. This study concluded that age has no predominant effect on the quantity or quality of intervertebral motion during flexion/extension, lateral bending and axial rotation for individuals under 60. Intervertebral disc degeneration increased according to age, especially at C5-C6 and C6-C7. Moreover, a more degenerated

spinal unit tended to have reduced mobility in asymptomatic individuals during flexion/extension and lateral bending. Levels adjacent to a severely degenerated level partially compensated the loss of motion.
A prospective assessment of the intermediate and long-term radiographic characteristics of disc replacement surgery with the Bryan Cervical Disc was completed in chapter 6. A correlation between the radiographic results with clinical outcome was made. The results of this analysis showed that the device maintained preoperative motion at the index and adjacent levels, seemed to protect against acceleration of adjacent level degeneration as seen after anterior cervical discectomy and fusion, and remained securely anchored in the adjacent bone mass on the long run. Moreover, it was observed that preoperative disc degeneration at the adjacent levels appeared to be a predictor for the further development of postoperative degeneration at those levels. However, heterotopic ossification at the index level was frequently seen. Nevertheless, the vast majority of all patients had a good to excellent clinical outcome, with postoperative mobility being positively correlated with clinical outcome. It should be noted that longer follow-up, i.e. up to 10 years after surgery and even more, is required before the added value of cervical arthroplasty compared to interbody fusion can be fully proven.
In chapter 7, quantitative and qualitative motion patterns of patients operated with a Bryan Cervical Disc Prosthesis were compared with a control group of healthy volunteers to investigate whether the maintained motion is normal and physiological. It was concluded that the Bryan prosthesis was able to mimic normal intervertebral ROM, continuous angular motion and a physiological center of rotation. This did not yield for AP translation and continuous translational motion. Nevertheless, both the quantity as quality of AP translation was maintained with respect to the preoperative situation after insertion of the prosthesis. Furthermore, the results suggested that the soft structures of cervical spine, e.g. ligaments and intervertebral discs, muscles, ... adapt to the changed biomechanics after cervical arthroplasty prior to stabilizing its motion patterns.
Chapter 8 compared postoperative segmental alignment between two cohorts of 20 consecutive patients operated with a Bryan Cervical Disc Prosthesis in a retrospective radiographic study. In one of the groups, patients with severe preoperative kyphosis were excluded for disc replacement surgery and the surgical technique was slightly altered in order to avoid asymmetric overdrilling of the posterior part of the cranial endplate of the caudal vertebral body. The aim was to investigate whether the change in patient inclusion criteria and the modification of the surgical technique had an influence on postoperative segmental alignment, and whether postoperative kyphosis is related to the mechanical properties and/or the design of the prosthesis. This study showed that segmental kyphosis with the Bryan Disc can be reduced and is therefore

not device related. Proper patient selection and a modified surgical technique can prevent this adverse outcome.
Finally, in chapter 9, the postoperative in vivo position of a cervical disc prosthesis was quantified in a retrospective radiographic analysis of a consecutive series of patients that were operated upon at C5-C6 and the influence of a malplaced prosthesis on the biomechanics of the cervical spine was investigated using a finite element model. Based on the results, it was concluded that optimal placement as advised by the manufacturer was not always obtained. Nevertheless these malplacements have a negligible influence on the mobility at the index and adjacent levels, on the stresses at the intervertebral discs, and on the contact forces at the facet joints of the adjacent levels. However at the operated level contact forces at the facet joint tend to increase if a prosthesis is not correctly positioned. This may eventually lead to accelerated facet joint degeneration at that level in the future. It needs to be mentioned that the current intact model and model with prosthesis has been validated against literature data solely. To improve the predictability e.g. in terms of patients specificity, additional validated against in vitro experiments may be needed.

In this thesis, the necessary tools were developed and methodologies tested to start the development of a biomechanical model that uses patient's radiographs or CT images and intervertebral motion patterns as input and that can suggest an appropriate prosthesis in terms of type, size, material properties, ... to ensure long term functioning of the device and to guarantee favorable long term clinical outcome and patient satisfaction.

10.1.2 Confirmation of hypotheses

Looking back at the first hypothesis of this thesis, which stated that proper patient selection in terms of preoperative mobility, the absence of pre-existing intervertebral disc degeneration at the index level and proper preoperative segmental alignment is imperative for long term postoperative mobility, and postoperative lordosis, the results presented in this work indicated that patient selection is indeed critical.
First, preoperative mobility at the index level increases the chances for the prosthesis to remain mobile after surgery. However, it needs to be noted that some patients regained mobility at the index level although they had limited or no mobility at the index level preoperatively. Furthermore, patients with postoperative mobile disc prosthesis tended to do better clinically.
Second, the existence of preoperative degeneration at the index levels showed to reduce mobility at that level.

Third, preoperative segmental kyphosis proofed to be baleful for proper postoperative alignment.
To conclude, if the goal is to have a patient that has a mobile prosthesis, does well clinically, and has a good lordotic alignment on the long run, the following selection criteria should be followed when considering cervical arthroplasty:

- Preoperatively, the patient should have a mobile index level.
- The patient should have minimal pre-existing degeneration at the index level.
- The patient should have a lordotic alignment prior to the surgery.

For patients have do not meet these inclusion criteria, anterior decompression and fusion might be considered as an alternative treatment. Whether postoperative malalignment is indeed associated with poor clinical outcome has not been confirmed in this thesis in should be addressed in future research. Moreover, the question regarding the amount of preexisting disc degeneration that is still acceptable for cervical arthroplasty could not be answered in this thesis.

A second hypothesis, namely that accurate implant positioning is essential to guarantee long term functioning of the prosthesis and clinical outcome, was also stated at the beginning of this thesis. The results suggested that surgical technique is crucial to obtain good postoperative segmental alignment, on the one hand. On the other hand, malplacement showed to have little effect on the mobility at the index and adjacent levels as well as on the stresses at the intervertebral discs, at least in the circumstance predicted by the FE model. However, it might predispose to accelerated facet joint degeneration at that level, and eventually pain at that level in the future. Therefore, one should bear the following suggestions in mind:

- Use the correct surgical technique to obtain proper postoperative alignment.
- Avoid intraoperative malplacement.

The surgical accuracy which is needed to obtain good clinical results was however not determined at this stage.

10.2 Future research

This multidisciplinary research collaboration was merely a first, but indispensable, step towards the confirmation of both hypotheses. Additional research is however required. In this thesis, several tools were developed which can serve as a base for future research. The following paragraphs provide suggested topics for future research.

Longitudinal prospective long-term radiographic follow-up

In chapter 6, the intermediate and long-term radiographic characteristics of disc replacement surgery with the Bryan Cervical Disc were assessed and correlated with clinical outcome up to 8 years after surgery. However, to draw final conclusions on the mobility, stability and functionality of the prosthesis, this patient cohort should be further followed up to at least 10 years after surgery. In this thesis, the tools were developed and a framework was established to complete this study. This data is of high importance and is anticipated in the field of cervical arthroplasty.

Validation of finite element model with in vitro experiments

As mentioned previously, any mathematical model, such as a finite element model, must be validated against experimental data to provide realistic estimations of the internal and external responses of the soft and hard tissues. Up to date, the developed finite element model was validated against literature data. However, validation against own in vitro experiments is essential. For this purpose, a surgical robot was modified to serve as load-controlled spine simulator. In these experiments, surgical inaccuracies in prosthesis placement can be introduced. Using intradiscal pressure measurements and three dimensional motion tracking of the vertebrae during loading, the results obtained with the FE model can be verified.

Refinement of finite element model

The FE model that was presented in chapter 9, was a first attempt towards the development of a biofidelic model of the cervical spine. Up to date, the vertebrae are modeled as rigid bodies. The introduction of deformable cortical and trabecular bone might provide further insight in the potential development of heterotopic ossification after cervical arthroplasty. Furthermore, the annulus was modeled using homogenized orthotropic cubic solid elements. The introduction of real composite material using fibres and matrix may generate a more physiological response and could answer question regarding the process of intervertebral disc degeneration. Finally, our results suggested that malplacement predisposes to an increase in facet contact force. However, in the current model, the facet joints are modeled using low friction cubic solid elements. The introduction of synovial fluid in the facet joint space might increase the predictability of the influence of a intervertebral disc prosthesis on the contact forces in the facet joints and increase the biofidelity of the model. With the refinement of the current model, the question regarding the amount of preexisting disc degeneration that is still acceptable for cervical arthroplasty might be answered. This question could be addressed by using the motion database of the healthy volunteers as input for the finite element model. This database provides information on how the individual vertebrae of a wide diversity of persons with differences in anatomy and differences in intervertebral disc degeneration move in all anatomical planes. To cope with this, the geometry of the model should me parameterized. Moreover, the effect of intervertebral disc degeneration on the mobility could be further explored. Next, it might be useful to not only look at the quasi static nature of the cervical spine, but to model the dynamic, viscoelastic nature of this complex structure. Subsequently, different material characteristic of the core of the prosthesis should be investigated. The E-modulus of the polyurethane has an important impact on the flexibility and stability of the prosthesis. The maximum stresses in the device could be compared to the yield stress of the materials to assure long term functioning of the prosthesis. Finally, the influence of prosthesis size should be assessed. It might be necessary to increase the current assortment to cope with the large interpatient variability.

The ultimate goal should be to develop a biomechanical model that uses patient's radiographs or CT images and intervertebral motion patterns as input and that can suggest an appropriate prosthesis in terms of type, size, material properties, ... to ensure long term functioning of the device and to guarantee favorable long term clinical outcome and patient satisfaction.

Edge impingement

In chapter 8, it was shown that postoperative kyphosis does occur but can be avoided using the proper surgical technique and be using stringent patient selection criteria. Kyphosis of the prosthesis is an important complication as it can be hypothesized that kyphosis leads to an accelerated wear of the prosthesis. Indeed, during flexion, prosthetic edge impingement might occur in a kyphotic prosthesis.

A future study might address the amount of needed lordosis of the prosthesis to avoid edge impingement. This can be predicted by assessing the amount of intervertebral rotation during anteflexion from neutral to full flexion preoperatively. Surgeons might use this assessment to adapt their surgical technique accordingly.

Instantaneous center of rotation

A database of intervertebral motion patterns of healthy volunteers and a cohort of Bryan patients was established in chapters 5 and 7. An extra parameter that characterizes invertebral motion in two dimensions, besides e.g. the range of motion, anteroposterior translation, continuous angular motion and continuous translational motion, is the instantaneous center of rotation (ICR). In literature, ICR is often wrongly attributed to the center of rotation of a FSU based only on full flexion and full extension data, without taking the intermediate flexion and extension positions into account. The instantaneous axis of rotation of a rigid body is defined as the instant axis through a point around which the body rotates and which is instantaneously motionless.
Because of the coupling between rotation and translation (tilting and sliding) during flexion/extension, the location of the ICR shifts posteriorly while performing retroflexion. This phenomenon can solely be demonstrated when the ICR is calculated based on a full sequence of flexion to extension images. When calculating the ICR, a compromise has to be made. The intervertebral angle between two frames of a pair of vertebrae needed to calculated the ICR, must have a certain threshold value (e.g. $>2^\circ$) to avoid numerical errors. Smaller angular steps, e.g. $<1^\circ$, tend to increase the errors in the ICR alarmingly.
The fluoroscopic image sequences of the healthy volunteers and the cohort of Bryan patients provide the data to assess and compare the ICR between both groups. Such an assessment can provide essential information towards the future development of implants.
The current image analysis techniques are not able to accurately calculated the ICRs. However, this might be possible using the aforementioned finite element model. The model does not suffer from measurement noise as the image analysis techniques do. As mentioned early, ideally such a model should be parameterizable to capture the difference in anatomy, and should be able to cope with the effect of intervertebral disc degeneration. If these criteria are met, the database of motion patterns of healthy volunteers would serve as an excellent input for that model, which in turn could calculate and predict the location of the ICRs.

Curriculum vitae

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